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Effects of Chronic Chitosan Salt Supplementation on Blood Pressure, Plasma Component, and Lipid Profile in Healthy Male and Female Adults

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Abstract   The effects of chronic chitosan salt supplementation on the systolic (SBP) and diastolic blood pressure (DBP), and physiological parameters were investigated in healthy male and female adult. Chitosan salt was conducted by measuring various health-related factors such as body composition, plasma Na^+, Cl^-, lipid, and lipoproteins profiles, glutamic oxaloacetic transaminase (GOT), and glutamic pyruvic transaminase (GPT) activity. Chitosan salt supplementation no significant differences before and after supplement in body composition variables and in SBP and DBP in either male or female. Plasma sodium and chlorine concentration no significant changes during chitosan salt supplementation, and no significant difference between two genders. Plasma GOT and GPT activity no different before and after supplement in either male or female. GOT activity significantly higher for male before supplement ($p<0.05$), and 2 weeks after supplement ($p<0.01$). The lipid and lipoproteins profiles of plasma no significant changes during chitosan salt supplementation in either male or female subjects. In summary, the chronic intake of chitosan salt did not affect the SBP or DBP, and posed no health risks.

Keywords: chronic chitosan salt supplementation, blood pressure, plasma component, lipid profile

Introduction

Solar salt is indispensable to human life. The human body contains 0.9% of salt in the blood, which facilitates human metabolism and purifies the blood vessels. In addition, salt plays an important role in physiological operations, such as creating blood corpuscles, maintaining the balance of body fluids by sustaining osmotic pressure, and helping with sterilization or digestion processes through its transformation into hydrochloric acid in gastric juice (1-3). The necessary amount of salt for an average human body is 2 g per day. This amount of salt can be obtained from the consumption of natural foods. In recent years, it has been reported that the Korean average daily intake of salt is about 15-20 g, which exceeds the average intake of 10 g in western people (4).

Salt is known to be a major factor in causing hypertension because excess sodium causes the absorption of excessive amounts of water into the blood in order to maintain a constant salt concentration in blood, which leads to the increased blood pressure. Eskimos in North America, who are known for consuming low-salt diets (4 g per day), exhibit the lowest rate of hypertension cases throughout the world. However, almost 30% of the people living in the northeastern provinces of Akida, Japan, who consume 33 g of salt per day, have hypertension (4). It is perhaps not coincidental that the high rate of hypertension

in Korea, 20%, is correlated with a daily salt intake of 15-20 g. The major reason why salt causes chronic degenerative diseases is not well known. It might not be due to the ingredients of salt itself, but rather to the harmful substances in salt which result from the contamination of the sea, where industrial and domestic wastes are discharged without being treated to remove toxic substances. Various diseases caused by excessive salt consumption result from sensitivity to excess Na ions, which relates to kidney function (5-8).

Some of the other ingredients in salt, such as K, Mg, and Ca ions, are thought to have positive effects such as expanding blood vessels, suppressing the secretion of aldosterone and renin, and restraining the action of angiotensin II. In addition, some studies have indicated that salt deficiency causes hypotension, exhaustion, anorexia, etc (9-12). Salts that are sold in current domestic markets are of two kinds: solar salt and refined salt. Refined salt is classified as purified and processed salt (13). Existing laws in Korea prohibit the use of solar salt as table salt and recommend using refined salt as table salt in which NaCl is extracted using an ion-exchange membrane. However, refined salt is problematic since some of the natural mineral ingredients of salt, which are vital to the human body, are removed in the process of refining. Actually, it is not possible to exclude salt, which is one of the most essential additives and preservatives in foods, from the diet (14, 15). Chitosan, which is proposed to have positive effects on controlling blood pressure and suppressing its increase (16), can be used not only in diets for people with hypertension, but also as a safe additive to

salt for general consumption.

This study evaluates the pathophysiological effects of 4 weeks of chitosan salt supplementation on systolic blood pressure (SBP), diastolic blood pressure (DBP), and its overall effects on healthy middle-aged male and female subjects.

Materials and Methods

Subjects The subjects participating in this study consisted of 10 adult males and 10 adult females, split into 2 groups based on gender. The groups are referred to as follows: 1) male chitosan salt supplement group, MCSG; 2) female chitosan salt supplement group, FCSG. Table 1 presents their physical characteristics.

Materials The material used in this study was chitosan salt, consisting of refined solar salt produced in Docho, Shinan, Korea containing 3% chitosan. The chitosan salt was then formed into tablets. The NaCl, moisture, total insoluble solid contents, and major trace components of chitosan salt were 93.80, 0.774, 2.740, and 2.686%, respectively.

Method of chronic chitosan salt supplementation All subjects were advised to maintain a normal diet. Chitosan salt was administered in the amount of 0.07 g/kg/day in the form of tablets. The chitosan salt tablets were consumed twice per day for 4 weeks. The subjects were advised to drink 1,000 mL of water per day along with the intake of chitosan salt. All subjects were assessed at 1 week intervals according to the experimental procedures.

Measurement of body composition Bioelectrical impedance analysis was used to evaluate body composition following chitosan salt supplementation. The bioelectrical impedance was measured and analyzed using a bioelectrical impedance analyzer (Kilwoo Trading Co., Seoul, Korea) by attaching electrodes on the wrist, back of the hand, instep, and ankle of the subjects, after spreading a type of gel at 5 cm intervals after the regions were cleaned with alcohol. The characteristics determined by this analysis were the impedance (ohm), body fat percentage (%), fat mass (FM, kg), fat free mass (FFM, kg), and total body water (TBW, L).

The measurements were conducted 5 times during the 4 week test period: immediately before chitosan salt supplementation, and after 1, 2, 3, and 4 weeks of

Table 1. Physical characteristics of subjects[1]

Item Group[2]	Age (yr)	Weight (kg)	Height (cm)	Suppl. amount (g)
MCSG(n=10)	41.30±4.11	72.58±8.45	172.92±6.83	5.14±0.59
FCSG(n=10)	36.50±2.68	55.54±6.98	157.30±4.28	3.95±0.49
t-value[3]	3.094**	4.914***	6.126***	4.094***

[1]Values are mean ±SD.
[2]MCSG, Male CHI supplement group; FCSG, Female CHI supplement group.
[3]**$p<0.01$, ***$p<0.001$, Significant difference between MCSG and FCSG.

supplementation. All values were produced using duplicate measurements.

Measurement of blood pressure The blood pressure of all subjects was assessed by measuring the SBP and DBP after sufficient rest on the morning of each test day. The blood pressure monitor used in this study was a mercury type sphygmomanometer (Matsushita Electrics, Osaka, Japan), and the blood classification was assessed according to the standard of the NIH (National Institute of Health), USA (17).

Blood sampling and analysis Blood sampling of the subjects was conducted after 12 hr of fasting on 5 occasions: immediately before chitosan salt supplementation, and after 1, 2, 3, and 4 weeks of supplementation. Ten mL of blood was collected from the antecubital vein of each subject using a disposable syringe and a vacutainer tube (Becton Dickinson, Franklin Lakes, NJ, USA), which was treated with ethylene diamine tetraacetic acid (EDTA). The collected blood samples were centrifuged for 15 min at 3,000×g (Centrifuge; Hanil 5000, Incheon, Korea), and the supernatant was transferred to an eppendorf tube and stored in a freezer maintained at -80°C until analysis.

An automatic blood chemistry analyzer (Vitro, DT 60 II; Johnson & Johnson, Somerville, NJ, USA) was used to analyze the plasma Na^+ and Cl^- concentrations, glutamic oxaloacetic transaminase (GOT), and glutamic pyruvic transaminase (GPT) activities, triglycerides (TG), total cholesterol (TC), high-density lipoprotein-cholesterol (HDL-C), low-density lipoprotein-cholesterol (LDL-C), and very low-density lipoprotein-cholesterol (VLDL-C) levels. All samples were measured in duplicate, and the mean values were used for further analysis.

Statistics Data obtained from this study were processed using the SPSS statistical package (V. 11.01) to produce the mean (M) and standard deviation (SD), and one-way ANOVA was used to examine changes over time during the chitosan salt supplementation period. Independent sample *t*-tests were conducted to examine the differences between each group. In addition, post-hoc tests (Newmann-keuls) were conducted for the measurements that showed a significance difference based on ANOVA. The level of significance used was $p<0.05$.

Results and Discussion

This study analyzed changes in body composition, systolic blood pressure (SBP), diastolic blood pressure (DBP), plasma electrolytes, liver function variances, and lipid and lipoprotein concentrations over 4 a week period of chitosan salt supplementation in 10 male and 10 female adult subjects. Table 2 presents the body composition values measured at 1 week intervals during the test period.

There were no significant changes in the subject's body composition during the 4 week test period for either the male or female subjects. However, there were significant differences between the two groups for each parameter. Significant changes in the body weight and percent body fat of the male and female subjects during the test period were not observed. These results are similar to those of a

Table 2. Body composition during chitosan salt supplementation[1]

| Period Variable[2]	Sex	Pre	1 week	2 week	3 week	4 week	F-value	p	post-hoc
Body weight (kg)	M	74.58±8.45	75.23±6.90	73.97±8.73	73.04±8.37	73.08±8.57	0.121	0.974	ns
	F	57.44***±6.95	56.45***±6.81	56.39***±7.00	56.17***±7.05	56.12***±6.96	0.059	0.993	ns
Imp. (ohm)	M	475.00±44.43	450.89±36.04	369.67±43.45	477.88±37.43	473.50±47.23	0.580	0.679	ns
	F	551.30**±57.01	539.00***±56.04	533.10*±63.69	525.20±59.29	549.70±50.03	0.371	0.828	ns
%fat (%)	M	23.94±3.75	22.70±4.22	23.76±4.24	24.55±4.70	24.17±3.87	0.270	0.895	ns
	F	27.96±5.88	27.49*±4.76	26.95±4.99	26.26±5.15	28.20±4.98	0.230	0.920	ns
FM (kg)	M	17.41±3.43	17.09±3.64	17.63±3.86	18.06±3.89	17.69±3.57	0.083	0.987	ns
	F	15.77±4.75	15.69±3.87	15.32±3.79	14.97±4.06	16.03±4.25	0.099	0.982	ns
FFM (kg)	M	55.11±6.72	58.14±6.04	56.33±6.97	54.98±5.66	55.39±6.95	0.366	0.831	ns
	F	39.76***±3.78	40.76***±4.21	41.07***±4.77	41.20***±3.96	40.09***±3.73	0.233	0.919	ns
TBW (L)	M	40.35±4.91	42.56±4.44	41.23±5.11	40.25±4.15	40.54±5.10	0.361	0.835	ns
	F	29.11**±2.77	29.83***±3.07	30.05***±3.49	30.15***±2.89	29.33***±2.73	0.229	0.921	ns

[1] Values are mean±SD; $*p<0.05$, $**p<0.01$, $***p<0.001$, significant difference between male and female; ns, no significant difference.
[2] FM, fat mass; FFM, fat free mass; TBW, total body water.

previous study in which animals were administered regular salt or chitosan salt for 8 weeks (16). The study reported no significant differences in the dietary intake, weight increase, and dietary efficiency with each salt supplement. This suggests that the intake of chitosan salt does not affect body weight or percent body fat.

Figure 1 and 2 present SBP and DBP measurements during the 4 week course of chitosan salt supplementation. Chitosan salt intake had no significant effect on SBP and DBP in either male or female subjects during the 4 week test period. However, the male subjects had significantly higher SBP and DBP values than the females throughout the test period.

It is known that hypertension has a very complex pathophysiological mechanism, and it has been suggested that the disease is caused mainly by genetic factors, insulin resistance, obesity, smoking, overdrinking, and excessive salt intake. Kurtz and Morris (18) reported that there was a decrease in blood pressure after reducing the intake of table salt, which lowered the maximum blood pressure from around 150 to 125±4 mmHg for 5 patients suffering from hypertension. The subjects were provided with ultra low salt food (0.58 g/day) for 1 week. After this period, they were served highly salted food (14.4 g/day) for 1 week and their maximum blood pressure increased to 142 ±4 mmHg. This shows that high salt intake results in an increase in blood pressure. Na and Cl are the major elements of salt, and there is disagreement about which element has the greater impact on hypertension. In order to identify which ion is most responsible for the increase in blood pressure, normal and spontaneously hypertensive rats were fed a high salt diet that contained vegetable fiber. There was an increase of Na in the excrement due to the alginic acid supplement; however the increased blood pressure caused by the high salt intake was not suppressed. The chlorine concentration in the blood decreased due to chitosan supplementation with a corresponding increase of chlorine in the excrement. The lowered chlorine concentra-
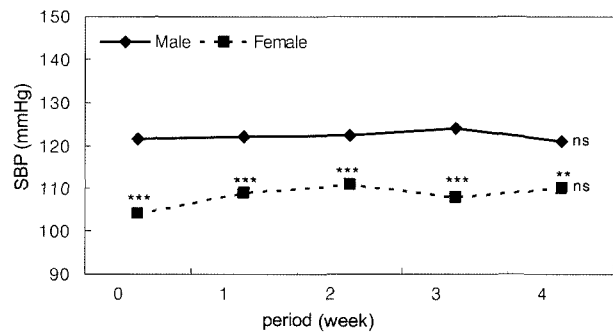
Fig. 1. Systolic blood pressure (mmHg) during chitosan salt supplementation. $**p<0.01$, $***p<0.001$, Significant difference between male and female; ns, no significant difference.
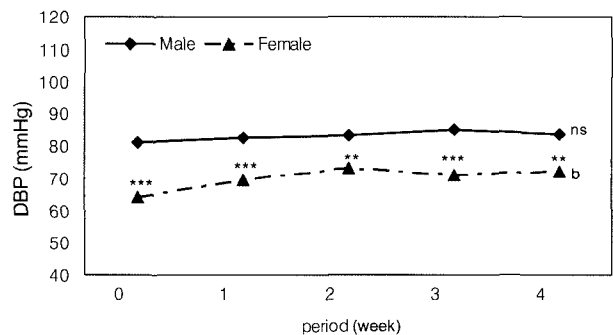
Fig. 2. Diastolic blood pressure (mmHg) during chitosan salt supplementation. $**p<0.01$, $***p<0.001$, Significant difference between male and female; b, $p<0.05$ significant difference between 0 and 2 weeks; ns, no significant difference.

tion in the blood suppressed the activity of angiotensin converting enzymes (ACE) in the blood. Thus, the intake of chitosan suppressed ACE activity by reducing the chlorine concentration in the blood. Thus, the lowered

chlorine concentration suppressed the blood pressure increase in both the normal and spontaneously hypertensive rats (19). This result is similar to the results of this study, in which the chronic intake of chitosan salt did not result in increased SBP and DBP for either male or female human subjects. These results are also supported by our previous study in which the chitosan salt supplementation resulted in a greater suppression of ACE activity than was observed with purified salt in male and female adults (20).

Figure 3 and 4 present the plasma sodium and chlorine concentrations during the chitosan salt supplementation period. The plasma sodium and chlorine concentrations exhibited no significant changes during the 4 week test period in either male or female subjects, and there was no significant difference between the male and female groups. These results differ from another study where chitosan and purified salt were supplemented for a short time. This study found that the concentration of Na^+ and Cl^- decreased significantly 60 min after supplementation with chitosan salt, but increased following supplementation with purified salt (20). In addition, other studies found that chitosan is an important factor associated with the

lowering of blood Cl^- ion concentration as well as blood pressure since chitosan, being a strong positive ion, adsorbs Cl^- ions (16, 21). Moreover, another study found that while the concentration of Na^+ ions increased following supplementation with 3% chitosan salt and did not change in response to a low salt diet, the Cl^- ion concentration following 3% chitosan salt supplementation was decreased relative to a control group. Even though some results from the current study are different from previous studies in that they did not show a significant change in ion concentrations, they are similar to another study which found that bamboo salt supplements (15 g per day) in addition to regular salt intake had no negative effects on blood pressure, and caused no significant changes in blood Na^+ and Cl^- ion concentrations (22). In order to evaluate the effect of chitosan in chitosan salt, it is necessary to compare the effects of chitosan salt supplementation with the effects of supplementation with purified salt.

Figure 5 and 6 show plasma GOT and GPT activities at different times during the period of chitosan salt supplementation. Plasma GOT and GPT activities remained
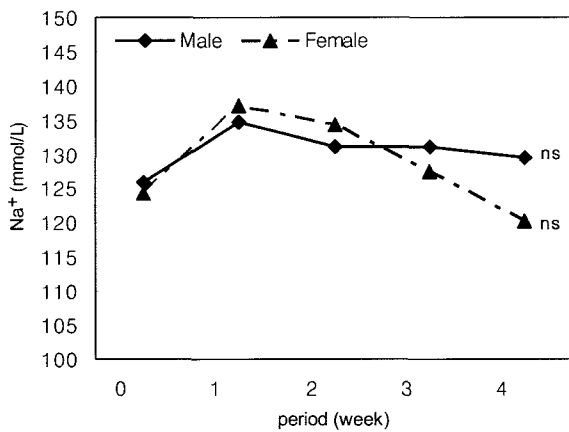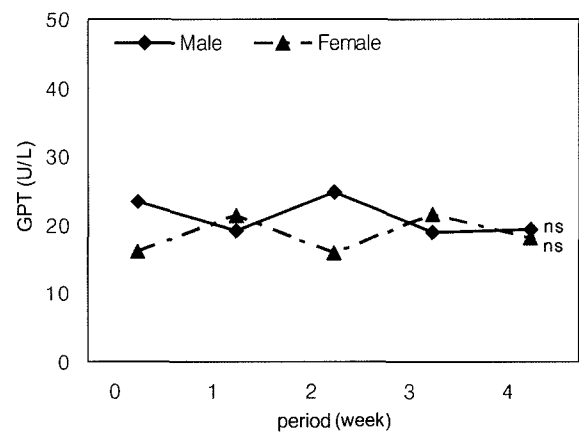

Fig. 3. Plasma Na^+ (mmol/L) concentrations during chitosan salt supplementation. No significant difference between male and female; ns, no significant difference.
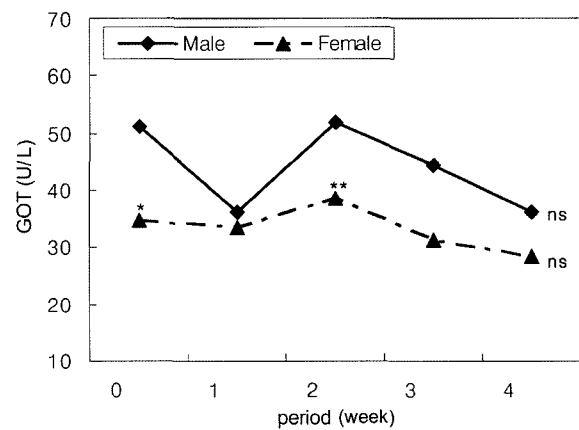
Fig. 5. Plasma GOT (U/L) activity during chitosan salt supplementation. $^*p<0.05,$ $^{**}p<0.01,$ Significant difference between male and female; ns, no significant difference.
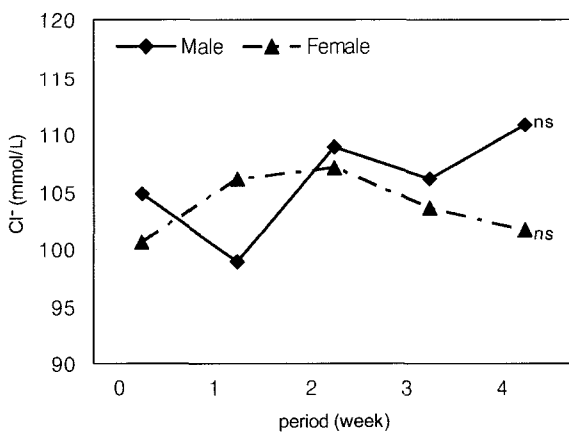
Fig. 4. Cl^- (mmol/L) concentrations during chitosan salt supplementation. No significant difference between male and female; ns, no significant difference.

Fig. 6. Plasma GPT (U/L) activity during chitosan salt supplementation. No significant difference between male and female; ns, no significant difference.

unchanged throughout the test period for both male and female subjects. The plasma GOT activity was significantly higher in males than females prior to chitosan salt supplementation ($p<0.05$) and 2 weeks into the test period ($p<0.01$). The other measurements revealed no significant differences between the two groups. Plasma GOT and GPT activities are commonly used as indicators of liver function. The normal ranges of GOT and GPT in the blood are both 0-40 IU/L. The plasma GOT and GPT activity values for the current study fell within the normal range and showed no significant changes during the period of chitosan salt supplementation, indicating that chitosan salt does not damage the liver.

Table 3 presents the plasma lipid and lipoprotein levels during the period of chitosan salt supplementation. The triglyceride (TG) concentration in the male subjects increased following chitosan salt supplementation, but the difference was not significant. In the female subjects, however, the TG concentration decreased during the first 3 weeks of supplementation, and then increased by the 4th week. The 4 week TG concentration of the females showed a significant increase ($p<0.05$) relative to the week 1 value. The males had significantly higher TG concentrations than the females throughout test period.

The concentration of total cholesterol (TC) remained unchanged in both male and female subjects throughout the 4 weeks of chitosan salt supplementation. In addition, there was no difference between the male and female groups during the test period except after 1 week ($p<0.05$).

The concentration of high-density lipoprotein-cholesterol (HDL-C) decreased gradually during the test period. There was a significant decrease ($p<0.05$) between HDL-C levels at the onset of supplementation and levels after 3 and 4 weeks in the male subjects. However, the female subjects exhibited no significant changes during the supplementation period. There was no significant difference between the values of the two groups.

The concentrations of low-density lipoprotein-cholesterol (LDL-C) showed no significant differences throughout the

test period in either male or female subjects. In addition, there was no difference between the two groups.

The concentration of very low-density lipoprotein-cholesterol (VLDL-C) showed no significant differences during the test period in the male subjects. However, the female subjects showed a significant increase ($p<0.05$) from the 1st to the 4th week. In addition, there was a significant difference between the male and female groups, with the female subjects having a lower level of VLDL-C than the male subjects. There were no significant differences in the TC/HDL-C ratios of male and female subjects during the test period.

In this study, while the concentrations of TG increased in both male and female subjects during the 4 weeks of chitosan salt supplementation, HDL-C concentrations decreased. Consequently, we concluded that the chronic intake of chitosan salt had a negative effect on lipid and lipoprotein metabolism. These results differ from a prior study, where the chronic supplement of chitosan salt decreased the TC compared to a control group (16, 23). In this particular study, while the group given regular salt showed a slight increase in TC, the group given 3% chitosan salt showed a decrease in TC (16). It is difficult to explain the reasons for the difference between these studies. Differences between the characteristics of the animals used in the previous study and the human subjects in this study were perhaps a factor. In addition, differences in the chitosan content, which was added to solar salt in the current study, and the amount of the supplement consumed, might also be important factors. A more accurate comparison would be possible if this study examined the effects of regular salt (purified salt) in comparison with chitosan salt. It is necessary to verify the lipid and lipoprotein characteristics by introducing a consistent amount of salt intake with consistent subjects, and to evaluate the clinical effects of purified salt in addition to chitosan salt.

Based on the results of this study, we propose that the chronic intake of chitosan salt, which showed no negative

Table 3. Plasma lipid and lipoprotein concentrations during chitosan salt supplementation[1]

Period Variable	Sex	Pre[a]	1 week[b]	2 week[c]	3 week[d]	4 week[e]	F-value	p	Post-hoc
TG (mg/dL)	M	142.44±67.29	144.00±75.44	169.4±86.15	159.89±114.13	197.00±95.68	0.614	0.655	ns
	F	69.89[**]±35.51	41.56[**]±8.22	46.44[***]±21.74	57.11[*]±33.31	89.56[**]±44.87	3.490	0.015	b-e
TC (mg/dL)	M	176.00±38.00	157.40±25.67	169.80±31.24	151.89±48.39	179.00±35.55	1.009	0.413	ns
	F	161.22±15.23	124.78[*]±27.10	137.56±38.22	153.67±29.08	184.00±38.82	2.068	0.103	ns
HDL-C (mg/dL)	M	62.00±25.53	48.40±21.99	41.10±12.57	37.00±15.22	36.60±8.15	3.464	0.015	a-d,e
	F	43.44±22.60	48.11±6.23	36.00±12.48	45.11±8.87	35.44±8.92	1.659	0.178	ns
LDL-C (mg/dL)	M	82.22±37.25	80.30±40.37	94.80±35.73	83.00±39.37	100.40±24.47	0.608	0.659	ns
	F	103.89±23.73	68.56±23.52	92.44±36.73	97.11±23.07	94.67±29.14	2.112	0.097	ns
VLDL-C (mg/dL)	M	28.56±13.45	28.70±15.24	33.90±12.35	31.89±22.67	39.20±19.03	0.597	0.667	ns
	F	13.89[**]±7.06	8.11[**]±1.69	9.11[***]±4.43	11.44[*]±6.63	17.89[**]±9.03	3.522	0.015	b-e
TC/HDL ratio	M	3.48±2.12	3.82±1.69	4.59±1.98	4.70±2.31	5.06±1.24	1.147	0.348	ns
	F	4.21±1.63	2.59±0.50	4.18±1.72	3.47±0.66	4.43±1.55	2.947	0.031	ns

[1]Values are mean±SD; [*]$p<0.05$, [**]$p<0.01$, [***]$p<0.001$, significant difference between male and female; ns, no significant difference.

effects on the blood pressure of male and female subjects, poses no health risks. Future studies may want to expand on this work by investigating changes in blood lipid and lipoprotein concentrations under more consistent conditions.

Acknowledgments

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