THE EFFECTS OF RED GINSENG ADMINISTRATION ON THE METABOLIC SUBSTRATES, SERUM ENZYMES AND STRESS HORMONES DURING EXERCISE

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INTRODUCTION

The most noticeable aspect of many physiological actions of Ginseng in the exercise physiology area is the action on cardiorespiratory system inclucing the chronotropic action of heart, the regulation of circulation and gas exchange etc. The second aspect is the metabolic action of Ginseng related to the utilization and mobilization of energy substrates including the enzyme system. The third aspect is the anti - stress action of Ginseng through the activation of hypothalamus - pituitary - adrenal axis.

There are many reports related to the effect of Ginseng on the cardiorepiratory system. for example, the inhibitory action of heart rate increase at same absolute load and the acceleratory action of the recovery of heart rate raised by exercise (Rhee & Nam, 1978 ; Forgo & Schimert, 1985) and hemodynamic improvement, such as. the decrease of blood pressure, the increase of cardiac output, venous return and central venous pressure during exercise (Kaneko, 1980 ; Hitoshi, 1983). Especially, Forgo (1983) and Dorling et al. (1980) reported the increase of maximal oxygen uptake followed by 12 weeks Ginseng extract administration.

In the aspect of energy metabolism, Bombardelli et al. (1979) and Hong(1975) reported that Ginseng extract ingestion prior to submaximal endurance exercise inhibited the depletion of endogenous glycogen storage in muscle and the formation of glycolytic metabolic substrates, lactate. The result was interpreted as the carbohydrate sparing effect of Ginseng through the inhibition of glycogen utilization as well as the stimulation of FFA oxidation in muscle at given submaximal exercise load (Avakian et al., 1984). Also, many reports suggested that Ginseng extract had insulin like effect and directly stimulated the synthesis and secretion of insulin from the Langerhan's island in Pancreas (Kimura et al., 1981 ; Okuda, 1984). In addition, in vitro and animal experiments suggested that Ginseng had hypoglycemic effect and the stimulatory effect of glycogenolysis in liver and the inhibitory effect of epinephrin induced lipolysis (Wang et al., 1990 ; Takaku et al., 1990).

In third aspect, Many researchers has suggested the conception that Ginseng inhanced the adaptive ability for various external stress including exercise by increasing the responsiveness of hypothalamus - pituitary - adrenal cortex to stress (Filaretov et al., 1988 ; Fulder, 1981). There are some reports that Ginseng ingestion stimulate the secretion of ACTH from the pituitary and the synthesis and secretion of corticosteroid by increasing C - AMP in adrenal cortex and also inhibit the depletion of cholesterol and ascorbic acid in adrenal induced from various stress, for instance, heat, cold, hypoxia, exhaustive swimming and injection of ACTH etc. (Pearce et al., 1982 ; Jang & Kang, 1981).

Therefore, the present study was done in order to offer the cue for the interpretation about the mechanism lying under the physiological effect of Ginseng as an ergogenic aid by the examination of the effects of 12 weeks Ginseng administration on the cardiorespiratory, metabolic system and HPA axis hormone responses to two types of exercise, maximal incremental exercise and submaximal continual exercise.

METHOD

1. Subject

The subjects were 23 adult male participating regularly in the physical activity of amateur soccer club, 34.23+2.83 yrs. They were randomly assigned to experimental group (E group : Ginseng administration group, N=11) and Control group (C Group : Placebo administration group : N=12). The physical, physiological characteristics of subjects are illustrated in Table 1.

Table 1. Physical characteristics of subjects

Items	Group	Experimental Group (N=11)	Control Group (N=12)
Age	(yr)	33.97± 2.79	34.83± 2.98
Height	(cm)	170.60± 3.42	169.14± 3.10
Weight	(kg)	66.48± 4.57	65.91± 4.94
HRrest	(bpm)	68.54± 5.98	66.72± 6.36
HRmax	(bpm)	188.18± 9.15	182.14± 11.44

Values are mean ± SD.

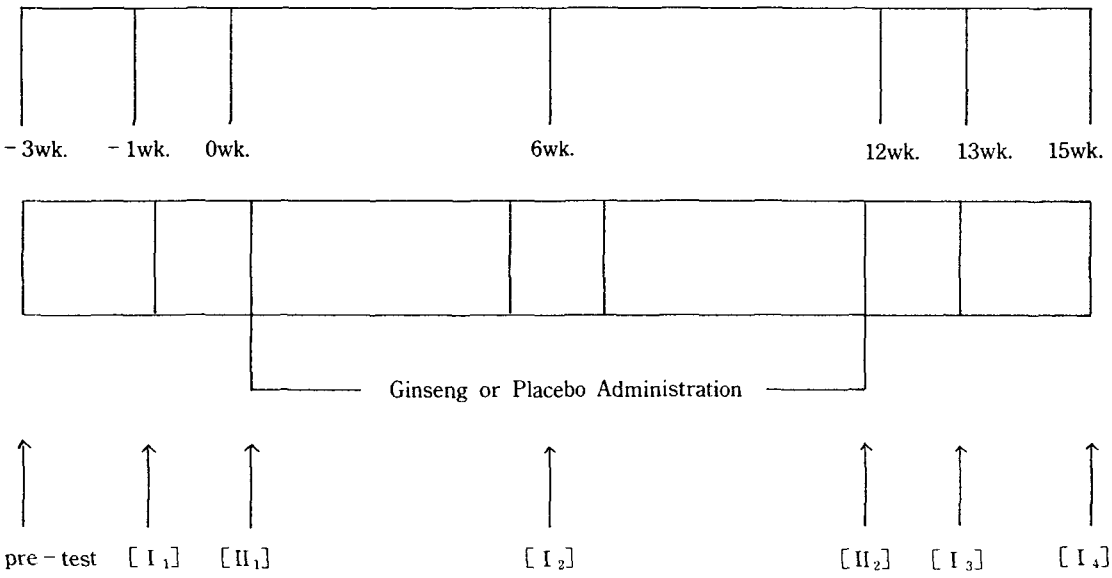
2. Procedure

1) Administration of Ginseng Extract

Group E (Ginseng administration group) received 50ml of solution containing 500mg of red ginseng extract and other additives such as Vitamin B complex, vitamin C, and electrolytes three times a day for 12 weeks. The solution, a drink type product, was developed and provided by the Korea Ginseng and Tobacco Research Institute. Placebo group received the same solution that E group received except Ginseng extract.

2) Experimental Protocol

All subjects were asked to perform two types of exercise on bicycle ergometer test I (incremental maximal exercise to exhaustion) and test II (continual submaximal exercise during 40 minutes at fixed load compromised to each subject's 65% VO_2 max)



* I_n ; gradual maximal exercise(experiment I)
II_n ; continual submaximal exercise(experiment II)
* The range of temperature and relative humidity during experimental period was 28.6-30.2℃ and 63~74%

Fig. 1. The whole process of experimental protocol

(1) Test I (Incremental Maximal Exercise Test)

All subjects in both Groups (N=23) performed maximal ergometer exercise four times (pre, 6 week, 12 week and 3 weeks after end of treatment). Blood samples were obtained only at pre- and 12 weeks-test. Each subject arrived at laboratory every one hour and after 30 min rest, resting heart rate, blood pressure and weight were measured. They were warm up with 50 rpm at 0 watt for 3 minutes and thereafter the work load was increased 25 watts every 2 minute until exhaustion. The heart rate and respiratory variables during exercise and 30 min-recovery period such as MV, VO_2 max, Anaerobic threshold, PWC_{170} time etc were obtained through the automatic gas analyzer (Erich Jaeger, German) and heart checker (Polar Electro, Finland). Blood samples during maximal exercise were taken from each subject's antecubital vein total seven times (pre-exercise, 8min, 12min during exercise, immediately after exhaustion, 3min, 10min after recovery) by catheter and analyzed for lactate.

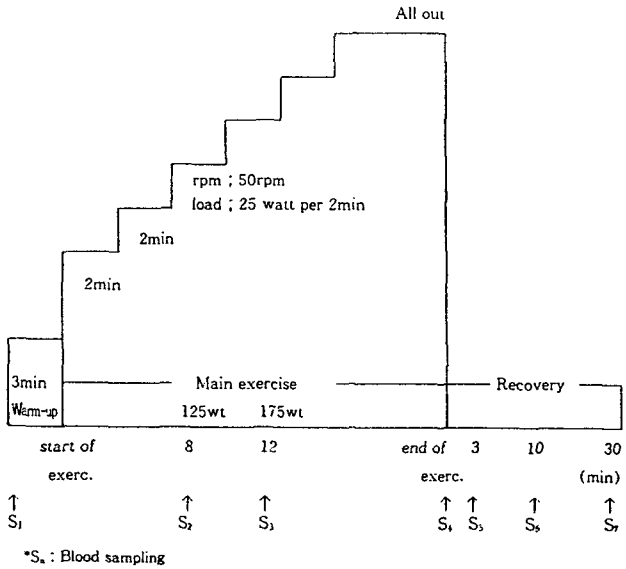


Fig. 2. Diagram of exercise protocol in experiment I

(2) Test II (Continual Submaximal Exercise Test)

Seven subjects from each group, total fourteen subjects were randomly selected for test II. The individual work load was determined as the load stage correspond to 65% of maximal oxygen uptake obtained from Test I (gradual maximal exercise). The warm up was performed during 3 minutes at 50 rpm and then the work load was increased 20 watt each minute until the individual fixed load correspond to each subject's 65% VO_2 max arrived. Thereafter subjects performed ergometer exercise at the fixed load during 40 minutes. The respiratory variables and heart rate were measured during 40 min - exercise and 30 min - recovery every 30 second. The 20ml of venus blood were drawn from subject's anticubital vein all five times (pre - exercise, 10min, 20min during exercise, immediately after exercise, and 30min after recovery) by catheter and analyzed for metabolic substrate (glucose, FFA, lactate), Enzymes (CPK, LDH and LDH Isoenzymes), and Hormones (Insulin, S - Endorphin, ACTH, Cortisol).

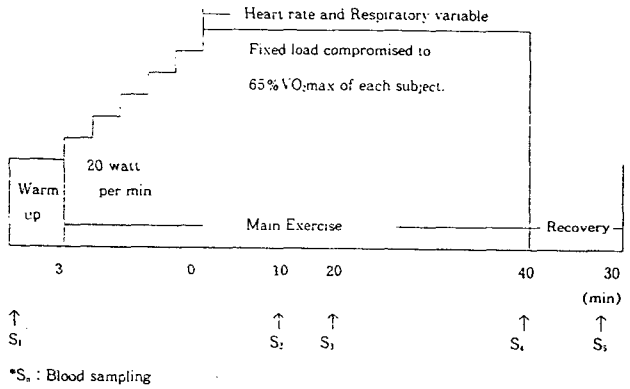


Fig. 3. Diagram of exercise protocol in experiment II

3. Calculation of Variables

1) Anaerobic Threshold (Ventilatory threshold)

During gradual maximal exercise, AT was determined as the absolute value of oxygen uptake or percentage to maximal oxgen uptake at the point of time that VE started to increase curvilineally while VO_2 increased in proportion to work load.

2) PWC_{170} time

During gradual exercise, PWC_{170} was determined as the time required until the subject's heart rate reached the 170 beats /min.

3) Recovery rate of lactate accumulation from maximal exercise

Recovery rate of lactate(%)

$$= \frac{\text{maximal lactate value} - \text{lactate value at 30min recovery}}{\text{maximal lactate value} - \text{resting lactate value}} \times 100$$

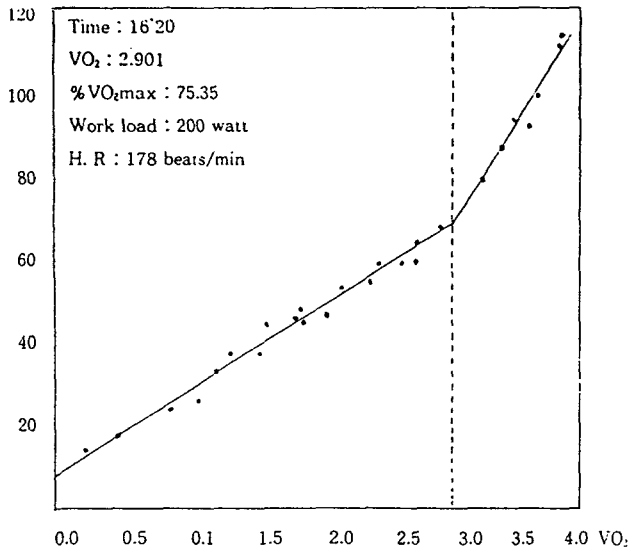


Fig. 4. Method of determining the ventilatory threshold.

4) Recovery rate of Heart rate from maximal exercise

Recovery rate of Heart rate(%)

$$= \frac{\text{maximal heart rate} - \text{heart rate at 5min recovery}}{\text{maximal heart rate} - \text{resting heart rate}} \times 100$$

5) Respiratory and Heart rate variables in Test II

Out of the respiratory data obtained every 30 second during 40min - submaximal exercise, the mean values of the interval from 29 to 39 minutes were selected as the data for analysis of this study in order to remove the effect induced from blood sampling procedure.

4. Data Analysis

The parameters were compared by 2 - way repeated ANOVA on the difference of the changes according to time course between two groups. The relationships between each variable were also examined by Pearson's coefficient of correlation. Difference and correlations were considered to be significant at 5% level ($p<0.05$).

RESULT

1. Respiratory and Heart rate variables

The VO_2 max was 41.35 + 5.67 and 37.78 + 6.92 ml/kg. min^{-1} in the experimental and control group, respectively. The values showed no significant change in two groups during all experimental period.

Ventilatory threshold significantly increased 9.57% in E group while in control group showed no significant change. Inspite of the difference response between two groups, no significant difference was not discovered.

Maximal heart rate, PWC_{170} time and Recovery rate of heart rate measured from gradual maximal exercise showed no signifi-

cant change during experimental period and also no significant difference between two groups.

During the submaximal exercise performed at the level of subject's 65% $\dot{V}O_2$ max, MV, O_2 pulse showed a little increase in E group and no change in C group through the experimental period. But there were no significant difference between two groups.

Although the changes of EQ O_2 and RQ were not significant, those parameters decreased somewhat in E group while increased a little in C group after 12 weeks.

Mean heart rate during submaximal exercise showed a significant decrease from 149.5+12.19 to 142. 6+11.85 beats/min in E group while there were no significant change in C group. Therefore, in the changes of mean heart rate a significant difference between two groups were discovered ($p<0.05$).

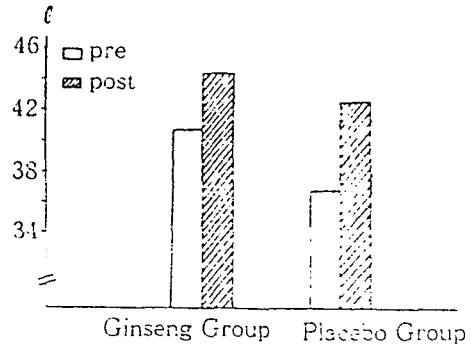


Fig. 5. The changes of mean ventilation volume during submaximal exercise in pre and post - administration

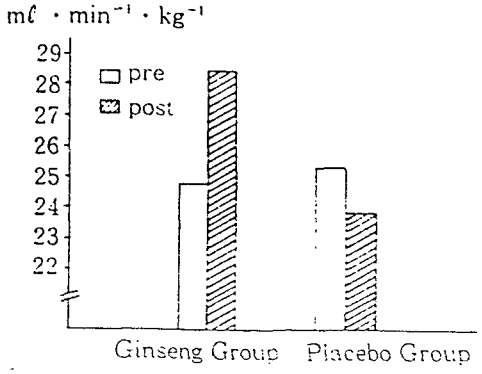


Fig. 6. The changes of mean oxygen uptake during submaximal exercise in pre and post - administration

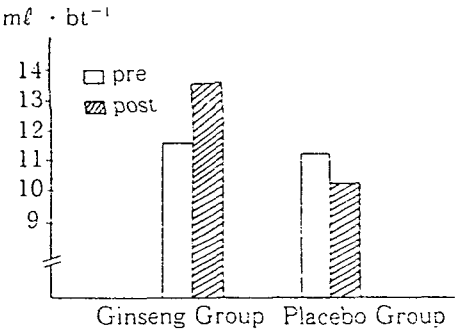


Fig. 7. The changes of O_2 pulse during submaximal exercise in pre and post - administration

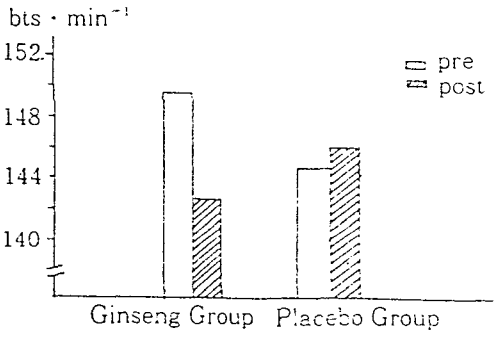


Fig. 8. The changes of mean HR during submaximal exercise in pre and post - administration

Table 2. The changes of various performance indices in submaximal exercise test. ($\frac{M}{SD}$)

		$\dot{V}(\ell)$	$\dot{V}O_2(\ell)$	$\dot{V}O_2(m\ell)$	O_2 pulse	mean HR	RQ	EQ O_2
	pre -	40.82	1.70	24.87	11.51	149.51	1.04	24.07
E Group	treat.	8.32	0.17	3.37	1.52	12.19	0.10	5.34
(N=7)	post -	44.20	1.96	28.50	13.37	142.61	0.94	22.71
	treat.	7.08	0.37	6.02	1.92	11.85	0.11	3.90
	pre -	36.88	1.61	25.46	11.23	144.78	1.03	22.84
P Group	treat.	9.04	0.36	3.54	2.67	16.25	0.11	4.37
(N=7)	post -	42.70	1.51	23.93	10.33	145.98	1.08	28.15
	treat.	6.65	0.11	2.54	1.19	17.26	0.06	4.56

2. Blood Metabolic Substrates

Blood glucose decreased consistently up to 20 min - exercise and thereafter increased again after the end of exercise and post 30 min - recovery. These glucose response phase to exercise showed no significant change even after 12 weeks in both groups and also no significant difference between groups. FFA showed no consistent change during submaximal exercise, but increased largely at the end of exercise and 30 min - recovery. These FFA change phase during exercise and recovery

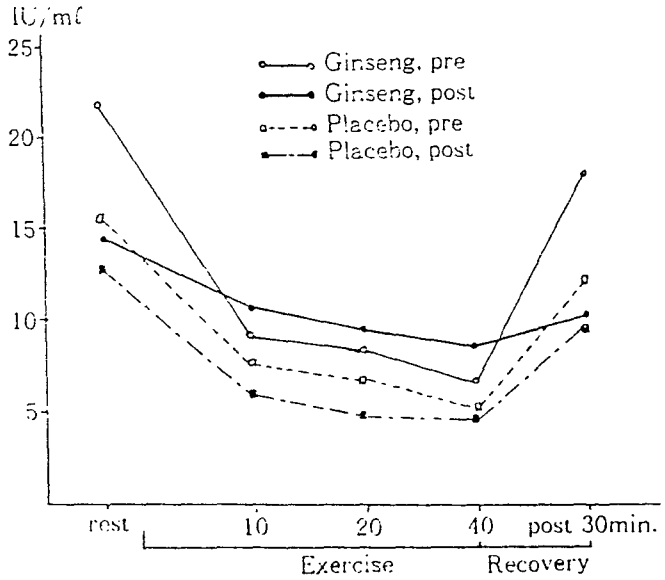


Fig. 9. The changes of insulin during submaximal exercise in pre and post - administration

was also not significantly different between two groups.

Insulin dicreased continually in both groups along with the time course during exercise and rebounded largely after 30 - min recovery ($p<0.05-0.01$). This insulin depression phenomenon during exercise was more remarkably alleviated in E group than in C group after 12 week - ginseng administration period ($p<0.05$). And blood lactate accumulation during gradual maximal exercise and recovery rate 30 min. after exercise showed no significant difference between both groups.

On the other hand, lactate accumlation at the end of continual submaximal exercise in E group decreased more significantly than in C group ($p<0.05$).

3. HPA axis Hormone Response

During submaximal exercise, the level of plasma β - endorphin slightly rised during exercise and declined below the pre - exercise level after 30 min recovery, but the changes were not significant statistically in both groups.

The level of plasma ACTH during exercise showed more slight increase at preexperiment than at post - experiment (after 12 weeks) in Ginseng group ($p<0.05$), but there were also no significant difference between Ginseng and placebo group.

The plasma cortisol also showed no significant changes during exercise and recovery in both groups and no difference between pre - and post administration was discovered.

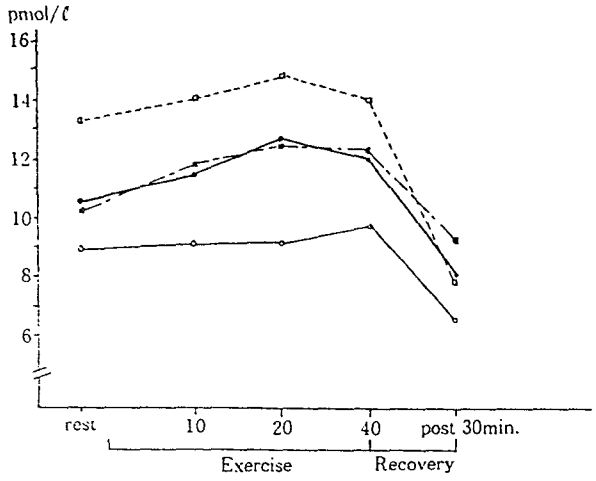


Fig. 11. The changes of β - endorphin during submaximal exercise in pre and post - administration

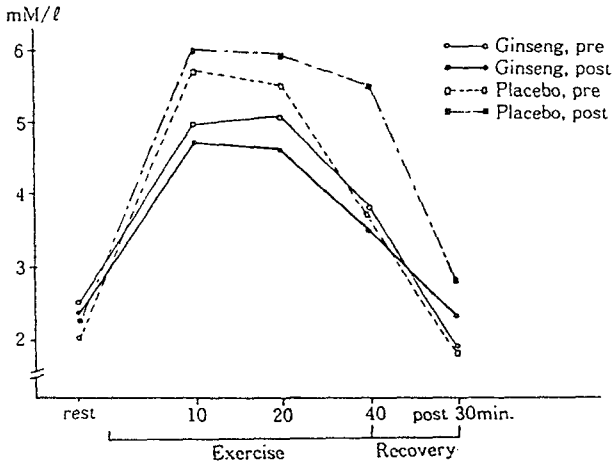


Fig. 10. The changes of lactate during submaximal exercise in pre and post - administration

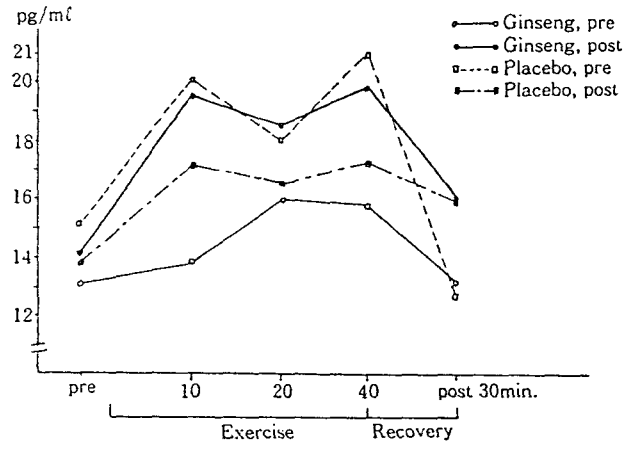


Fig. 12. The changes of ACTH during submaximal exercise in pre and post - administration

4. Serum LDH, CPK and LDH Isoenzyme

The serum LDH and CPK during maximal and submaximal exercise were significantly increased along with the time course in both groups, but the difference of the enzyme responses between two groups were not discovered during all experimental period. During exercise, the percentage of the H type LDH Isoenzyme (LDH_1 and LDH_2) decreased remarkably while the percentage of M type LDH Isoenzyme (LDH_5) increased continually over the pre-exercise value.

In consequence, the ratio of H type/M type showed significant decrease during exercise in both groups ($p<0.05$). This phenomenon that the ratio decreased during exercise was considerably alleviated in E group compared to C group, but no statistical significant difference between two groups was discovered.

DISCUSSION

In this study, Although the performance indexes, such as, the maximal heart rate, maximal oxygen uptake, ventilatory threshold, PWC_{170} time measured during gradual maximal exercise showed somewhat improvement after 12 weeks in E group, there was no significant difference of the change between two groups. On the other hand, the mean heart rate obtained during continual submaximal exercise reduced more significantly in E group than in P group ($p<0.05$). These results indicated that 12 weeks ginseng administration exerted more remarkable inhibitory effect on the central nervous system at submaximal exercise than at maximal exercise.

The inhibitory effect of ginseng on heart rate during exercise and the acceleratory effect on heart rate recovery after exercise has been reported by many studies (Dorling et al., 1980 ; Lee, j.k., 1974). Besides, these results appear to suggest that the long-term ginseng administration reduce the tone of the sympathetic activity accelerated by exercise and act as a adaptogen to alleviate the load imposed on the heart during exercise like the acute administration.

Kaneko et al(1984) reported the acute ginseng administration before exercise in 24 males and females inhibited the increase of heart rate during exercise and reduced the depression degree of ST segment on electro-cardiograph and they explained the results as the effect of ginseng saponin sparing the oxygen consumed by the heart muscle as well as the effect improving the coronary circulation.

A series of the experiments done by Forgo (Forgo & Schimert, 1985 ; Forgo, 1983 ; Forgo & Kirchdorfer, 1981) reported consistently the increase of maximal oxygen uptake, O_2 pulse, FV_1 etc after a given long-term ginseng administration. They

Table 3. The changes of LDH isoenzymes during submaximal exercise in two groups. ($\frac{M}{SD}$)

Group		BS	Rest	Exercise			Re-30
				10 min	20 min	40 min	
E Group (N=7)	pre						
	LDH_1		29.41	28.54	28.50	28.62	29.88
	LDH_2		42.01	40.27	38.41**	38.92*	40.88
	LDH_3		12.37	13.48*	13.80*	14.03	13.24
	LDH_4		5.12	5.94*	6.67*	5.80	4.94
	LDH_5		11.22	11.74	13.21**	12.80*	11.04
	post						
	LDH_1		29.02	27.60	26.42*	27.95	26.91
	LDH_2		38.34	37.40	38.08	37.82	39.36
	LDH_3		17.60	17.74	17.85	17.63	17.08
	LDH_4		6.01	5.85	6.81	6.41	6.58
	LDH_5		8.71	9.41	10.72*	10.14	9.91
P Group (N=7)	pre						
	LDH_1		33.33	31.15*	29.30	31.08	32.55
	LDH_2		42.07	40.97*	39.47**	40.61	41.62
	LDH_3		12.16	14.04**	14.12*	13.11	12.85
	LDH_4		3.00	4.18*	5.84**	4.34	3.44
	LDH_5		9.34	9.62	11.18	10.85	9.48
	post						
	LDH_1		31.95	29.20	28.54**	28.54*	26.28**
	LDH_2		38.34	36.74*	37.80	37.98	38.78
	LDH_3		16.55	18.54*	18.12	17.82	18.42
	LDH_4		5.31	6.28*	6.27	6.27*	6.78*
	LDH_5		7.81	9.27	9.28	8.84	9.70**

* $p<0.05$, ** $p<0.01$, $p<0.01$ as compared with pre-exercise value.

indicated the hypothesis that the improvement of the respiratory variables may be associated with the arterial oxygen tension, but the hypothesis has not been proved yet.

Several reseachers has reported that Ginseng administration before exercise inhibited the depletion of endogenous glycogen storage and the formation of glycolytic substrates such as lactate, pyruvate during exhaustive endurance exercise (Brekham ; 1969, Avakian, 1979).

They suggested that the rusults were due to the inhibitory action of ginseng on the glycogenolysis and the stimulatory action on the aerobic synthese of ATP through the lipid oxidation in muscle. In this study, the insulin depression phenomenon during exercise was remarkably alleviated in E group after 12 weeks while there was change in C group. This result is alike to the typical phenomenon discovered in trained people compared to untrained people (Holloszy, 1984 ; Pederson, 1984).

Many studys suggested that glycans DPG - 3 - 2, adenosine of Ginseng components has insulin - like effect inhibiting the catecholamine induced lipolysis in adipocyte (Yeung, 1985 ; Takaku et al., 1990) and also the action stimulating insulin synthese and secretion in Langerhan's island of Pancreas (Kimura et al., 1981 ; Ando et al, 1979).

In this study, the lower lactate accumulation during submaximal exercise in E group appeared to suggest that long term Ginseng administration might stimulate repeatedly the depletion of liver glycogen by the glycogenolysis and so stimulate the replenishment of liver glycogen and increase the storage of muscle glycogen and by stimulating the insulin synthese and secretion and consequently contribute to more dependancy on lipid oxidation as energy sourcse at the given level of exercise intensity. These results were accord with many other studies reported the lower lactate accumulation and the noticeable delay of exhaustion time followed by Ginseng administration (Hong, 1975 ; Forgo & Schimert, 1985).

The anti - stress mechanism of Ginseng was known to be responsible for the stimulatory action of saponin on the activity of hypothalamus - pituitary - adrenal cortex axis (Filaretov et al., 1988 ; Hiai et al., 1979). But we could discover no evidence that HPA axis activity (β - endorphin, ACTH, cortisol) significantly increased during exercise after 12 week ginseng administration. These descrepancy appears to be caused by selecting the insufficient exercise intensity below the secretion threshold of HPA axis hormones and the different ginseng ingestion method from the preceding studies.

Unlike this study, most preceding studies selected the animal as subjects and the acute oral or subcutaneous ingestion method of ginseng extract imediately before exercise and imposed the forced endurance exercise on subjects until exhaustion. In general, the increase of serum enzyme level during acute exercise was known to be induced by the increase of permeability and demage of muscle cell membrane caused by intracellular hypoxia (Stansbie et al., 1983). Therefore, the response of the enzymes such as CPK, LDH to acute exercise had ever been proposed as a useful index of stress applied by exercise (Nuttall & Jones, 1968).

We expected that long term ginseng administration might inhibit the increase of these serum enzymes according to maximal or submaximal exercise. But we couldn't discover the significant difference of these serum enzyme responses between Ginseng group and Placebo group. Only, we observed the result that the increase of M - type LDH (LDH_5) according to exercise was more remarkably alleviated after 12 weeks in Ginseng group compared to Placebo group, but there was no statistical significant difference.

CONCLUSION

On the basis of the results analyzed in this study, the conclusion could be drawn as follows :

1. Mean heart rate during submaximal exercise in Ginseng Group was significantly lowered after 12 weeks compared to Placebo Group ($p<0.05$). But, other respiratory and heart rate variables during two types exercise showed no significant difference between two Groups.
2. Plasma insulin depression tendency during submaximal exercise in Ginseng Group was significantly alleviated after 12 weeks compared to Placebo Groups ($p<0.05$). Enery substrates (plasma glucose, FFA) changes were not significantly different from Placebo Group.
3. Lactate tolerance (peak lactate accumulation), Lactate recovery rate during maximal exercise and recovery period were not significantly changed after 12 weeks in two groups. But, in submaximal exercise, the significant difference in plasma lactate change between two groups was discovered in pre - 40 min time interval from T test ($p<0.05$).
4. Plasma β - endorphin, ACTH and cortisol response during submaximal exercise in pre and post - administration showed no significant difference between two groups.
5. Serum LDH and CPK responses to submaximal exercise showed no significant difference between two groups. Although the statistical significance of the change was not discovered, LDH Isoenzyme changes during exercise (decrease in H type and increase in M type Isoenzyme) were alleviated after 12 weeks in Ginseng Group.

The noticeable results in this study were that 12 - week ginseng administration effected the mean heart rate and lactate accumulation during submaximal exercise. This result suggests that ginseng may more contribute to the alleviation of metabolic acidosis in submaximal exercise than in short - strenous anaerobic exercise and the alleviative action may be achieved by the increment of feul storage in muscle and liver through the improvement of insulin secretion ability rather than through the response of HPA axis hormones or metabolic role of serum CPK, LDH and LDH Isoenzyme.

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