KOREAN RED GINSENG IN EXHAUSTION EXERCISE

J.G. Prieto, E. Fernández, P.A. Redondo, A. Ferrando, L. Vila, J. Voces, del J. Estal and A.I. Alvarez

Lab. of Animal Physiology. Dpt. of Physiology, Pharmacology and Toxicology. University of Leon, Spain.

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ABSTRACT

The effects of Korean Red Ginseng (KRG) in rats submitted to exhaustion exercise have been studied, by measuring different enzymatic and hematological parameters in plasma and muscle.

KRG powder was daily administered to 15 male Wistar rats for a period of two weeks. Another group of 15 rats with the same characteristics were administered physiological saline.

Both groups were divided as follows : 5 control, 5 exercised till exhaustion and 5 recovered for 48 h after exhaustion.

The following results were obtained for the groups treated with KRG in rapport to those treated with saline :

- Higher endurance to running.
- Increase of the osmotic resistence of red blood cells and higher presence of reticulocytes.
- Lower triglyceride levels in plasma.
- Increase non statistically significant of urea levels in plasma.
- Lower non statistically significant hypoglycemia after exhaustion exercise.
- Decrease of liver glycogen after exercise and faster recovery of the resting - level.
- Protective effect on tissular damage produced by exhaustion exercise
- Lower LDH activity in all studied muscles, only statistically significant in the WG.

INTRODUCTION

A large number of studies about the relevant role played by the physiological adaptations to prolonged or exhaustion exercise have been carried out, both in sedentary individuals and athletes as well as in experimental animals. The existence of an increase in the respiratory capacity and in mitochondrial enzymes levels in muscle - in response to endurance training - is clear.

Prolonged endurance and exhaustive exercise induce changes in the enzyme pattern of energy metabolism in muscle fibers. The absolute activity levels of enzymes involved in aerobic and anaerobic metabolism, produce markedly altered ratios of the main system of energy supply (Green et al. 1983 ; Tesch et al. 1989).

The main metabolic changes in exhaustive exercise involve glycolytic enzymes and Creatine Kinase (CK) in mixed muscles, and oxidative enzymes in red muscles. The increase in the oxidative capacity of skeletal muscle in response to an acute endurance exercise, drops gradually to the resting - level during the 48 h post - exercise period in rats (Takekura & Yoshioka. 1988).

It is well known that, during exercise, there is a sharp depletion of muscle glycogen in men. Similar results have been obtained in rats in a differential way, according to the type of muscle involved (Baldwin et al. 1973). It is known that in rats, the liver must prevent hypoglycemia caused by the exercise induced increase in glucose utilization by skeletal muscle. During heavy exercise, the liver produces glucose primarily by glycogenolysis (Winder, 1985). On the other hand it is also known that after exhaustion exercise, there is an important glycogen resynthesis in the different muscular fiber types and, consequently, in the liver (Johnson & Bagby, 1988 and Vollestad et al. 1989).

As shown by Spodaryk et al. (1989), physical exercise leads to an increase in reticulocyte and young erythrocyte counts in the peripheral blood, also bringing an increase in intravascular hemolysis and removal of older red blood cells from circulation. Similar experiments described that red - cell osmotic fragility was similar in control and trained subjects (Spodaryk et al., 1990). The Red Blood Cells count (RBC), Hematocrit (Hc) and Hemoglobin (Hb) concentration were lower in endurance athletes than in control subjects.

In an attempt to extrapolate the results obtained in rats to humans, it must be considered that, in rats, most mitochondrial enzymes levels are much higher in the fast - twitch red fibers (Type IIa) than in the slow - twitch red fibers (Type I) and in the fast - twitch white fibers (Type IIb), Holloszy & Coyle (1984). On the contrary, in humans, the type I fibers have the highest content of mitochondria.

The Ginseng is a complex with beneficial effects on physical performance, not only as a dietetic supplement but as a treatment of physical fatigue. In a controlled exercise protocol with athletes, a significant increase of hemoglobin and VO_2 and a decrease of LDH serum levels have been found, improving both the aerobic and anaerobic capacities of the athletes (Alvarez et al. 1990).

Our research team (Laboratory of Animal Physiology, University of Leon, Spain) has been working on the relation between anabolic steroids and sports, in order to determine the values of physiological parameters - enzymatic and hystochemicals - in muscle and plasma. Considering that the use of anabolic substances is forbidden in sports, due to its negative collateral effects, and that the use of Ginseng improves physical performances, our objective is to investigate - as a first step - the beneficial effects of the administration of Ginseng on several physiological parameters involved with hematological profile and muscle enzyme activities related to fatigue, muscular damage and recovery

after exhaustive exercise.

KRG - Panax Ginseng C.A. Mayer - manufactured by Korea T. & G. Co., Republic of Korea. has been chosen due to its high quality.

MATERIALS AND METHODS

The study was carried out on 30 male Wistar rats with an average body weight prior to treatment of 260± 30g, distributed randomly as follows :

Without Ginseng :

The animals were daily given 1 ml of physiological saline by forced oral administration.

- L1 : 5 animals control.
- L2 : 10 animals. They were exercised till exhaustion. Half of them were killed and analysed at the end of the experiment (Exhaust. group), while the other part was recovered for 48h after exhaustion and killed before being analysed (Exhaust. + Rec. group).

With Ginseng :

The animals were daily administered 50 mg/kg body weight of KRG root powder dissolved in saline, following the same procedure, for a period of 2 weeks - one prior to the training protocol, and the other during it.

- L3 : 5 animals control.
- L4 : 10 animals. They were exercised till exhaustion. Half of them were examined at the end of the experiment (Exhaust. group), while the other half was recovered for 48h after exhaustion and killed before being analysed (Exhaust. + Rec. group).

Exercise protocol :

The control groups (L1 and L3) were trained by means of a program of Treadmill running (Letica, L1 8706) for a period of 7 days ; the duration of running was 5 min/day, at a running speed of 9 m/min and a 0% slope, in order to simulate the stress situation created by Treadmill running, as did the rest of the experimental groups.

Groups L2 and L4 were trained to Treadmill running according to the following protocol :

1st Day : 5 min at 9 m/min and 0% slope
2nd Day : 10 min at 9 m/min and 10% slope
3rd Day : 20 min at 12 m/min and 10% slope
4th Day : 30 min at 12 m/min and 15% slope
5th Day : 45 min at 15 m/min and 15% slope
6th Day : 60 min at 15 m/min and 15% slope
7th Day : The training ended with an Exhaustion Exercise consisting of :
2h at 15 m/min and 15% slope
1h at 24 m/min and 15% slope

After the exhaustion exercise, half the animals of groups L2 and L4 were killed and immediately analysed, and the other half were allowed to recover for 48 h before examination.

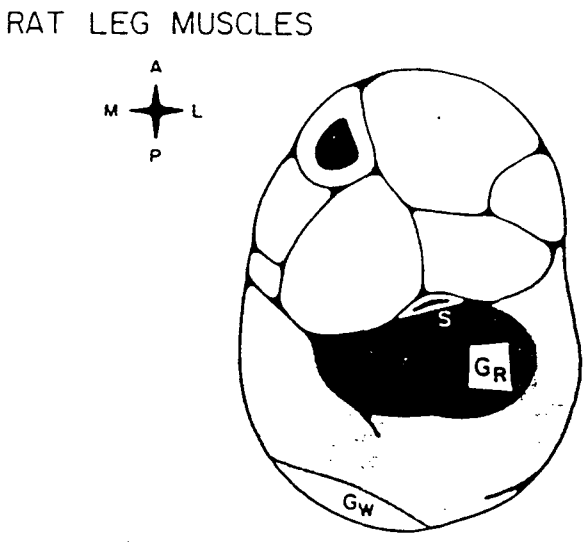
Samples preparation :

At the end of the experimental protocol in each case, 5 ml blood samples were taken by cardiac puncture. Part of the samples were used to study the osmotic fragility and to determine the RBC, Hc and Hb by means of a Coulter Counter. Reticulocytes were stained with brilliant cresyl blue and counted on a smear to be expressed as the percentages per 1000 cells. Later, the percentages were corrected on the basis of red - cell count(hematocrit).

Other part of the blood samples was centrifuged and the plasma was stored at -80℃ for further utilization. Assessments of Glucose, Total Cholesterol, Triglycerides, Creatin Phosphokinase, Alkaline Phosphatase, Lactate Dehydrogenase (LDH), Aspartate - aminotransferase (AST or GOT), Alanine - aminotransferase (ALT or GPT), Urea and Total Proteins were estimated in this plasma by commercial tests.

Afterwards, the Soleus and Gastrocnemius muscles of both hindlimbs were excised, weighed and stored at -80℃ for further examination. The muscles were dissected following the indications of Armstrong & Laughling (1985), (Schema 1), obtaining on one hand the Soleus and, on the other, the White Gastrocnemius (GW) and the Red Gastrocnemius (GR), in order to get a representation of muscles mainly constituted by Type I fibers (oxidative fibers), Type II fibers (glycolytic fibers) and Type I & II fibers, respectively.

Finally, a laparatomy was performed, and the liver was perfused with physiological saline through the porta vein, being extracted, wheighed and stored at -80℃ in 1g fractions for further analyses.



Schema 1. Cross - sectional view of the rat hindlimb showing the location of the Soleus (S), Red Gastrocnemius (GR) and White Gastrocnemius (GW).

Five ml of $HClO_4$ at 2% were added to 1g of liver and homogenized, being centrifuged for 10 min at 3000 rpm (1086 g) in a Jouan BR-311 at 4℃. The hepatic glycogen, according to the technique of Keppler & Decker (1974), was determined in supernatant.

Muscle enzyme analysis :

To determine the enzyme activities of the muscles, they were homogenized 1 : 19(w/v) in 50 mM-TRIS/HCl buffer, pH=7.4, containing 2 mM-Titriplex and 2 mM $MgCl_2$.

Enzymes were analysed in supernatant after being centrifuged for 20 min at 3000 rpm.

Muscle Lactate Dehydrogenase - cytosolic enzyme of glycolysis - was determined by the method of Kornberg (1955).

Citrate Synthase was determined by the method of Srere (1969).

Protein contents per gram of muscle were measured by the method described by Markwell et al.(1978).

Enzyme activities in muscle preparations were then expressed as units of enzyme activity per mg of supernatant protein.

Hemolysis curves :

Blood samples in each experimental group were analysed using 3 replicates, with a series of stock hypotonic hemolysis solutions within the range between 20 - 115 mM NaCl. Heparinized fresh blood (50 μl) was incubated at 37 ℃ for 60 minutes after gentle mixing with 5 ml of the stock hemolysis solution. An additional test solution containing destilled water was added as a positive control (100% lysis). The tubes were centrifuged for 10 min at 3000 rpm, and optical density of the released hemoglobin in the supernatant was measured at 540 nm in a spectrophotometer (Milton Roy Spectronic 1201). The absorbance at 540 nm was directly proportional to the hemoglobin concentration. To find the percentage of hemolysis, the absorbance of each test value sample was divided by the absorbance of the totally lysed sample and multiplied by 100.

Hemolysis curves (hemolysis fraction vs. NaCl concentration) were obtained from the experimental hemolysis data, according to the procedure described by Detraglia et al. (1974).

Statistical procedures :

To determine the effects of KRG on the exhaustion exercise and the recovery after 48 h, an analysis of variance was performed. Where significance was indicated, a post-hoc analysis - with the use of the LSD test - was performed in order to compare specific means.

Where only two experimental groups were compared, as with the H_{50} data, the Student's test for correlated samples was used.

A 95% level of confidence was accepted for all comparisons.

RESULTS AND DISCUSSION

The duration of the exercise required to attain exhaustion was : for L2 group (without KRG) 2h and 19± 8 min, and for L4 group(with KRG) 2h and 43± 15min. Such results present statistically significant differences.

As for the study of variations in osmotic fragility, there is a remarkable increase in the osmotic resistance of red blood cells(lower H_{50}) in the groups where KRG was administered (Memolysis Curve displaced to the left), already evidenced in the control group. This tendency is kept in the other experimental groups (Fig. 1A).

β parameter as a measure of the RBC population distribution is higher in the groups treated With Ginseng, although this difference is statistically non significant, which will indicate a minor variation of eritrocitary populations liable to hemolysis (less wide distribution curve) (Fig. 1B).

The Red Blood Count, Hematocrit and Hemoglobin show

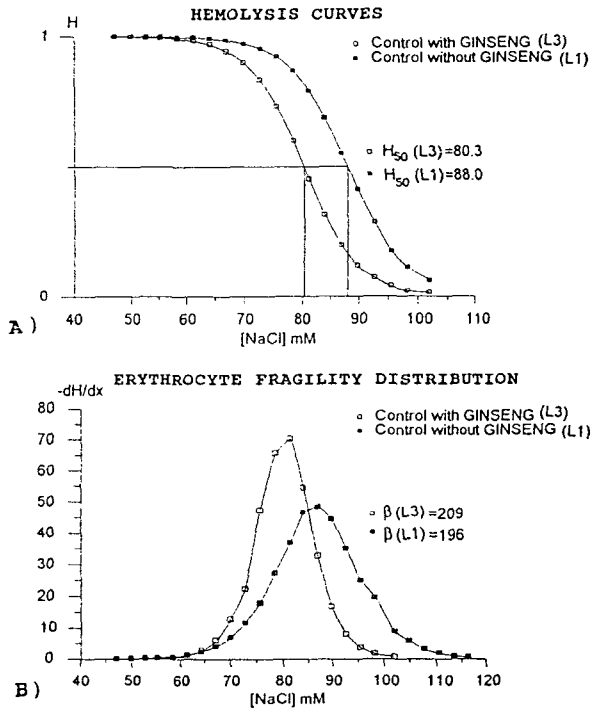


Fig. 1. Hemolysis curves and H50 values (A) and Erythrocyte fragility distribution (B) for control groups (With and Without KRG).

	H_{50}		β
With Ginseng			
Control	80.3± 0.6*		209.06± 26.10
Exhaust.	79.0± 0.3*	*	290.33± 24.24
Exhaust.+Rec.	76.8± 0.2*		303.97± 19.30
Without Ginseng			
Control	88.0± 0.4		196.03± 17.50
Exhaust.	85.5± 0.3	*	190.24± 13.23
Exhaust.+Rec.	74.0± 0.3		239.87± 15.69

* Statistical significant differences($p<0.05$) when each group of GINSENG is compared with the corresponding group without GINSENG.
* Statistical significant differences ($p<0.05$) between the different groups of each treatment

Table 1. Values of RBC, Hc, Hb and Reticulocytes in blood samples for all experimental groups.

	RBC 10^6/μl	Hc(%)	Hb(g/dl)	Retic.(%)
With GINSENG :				
Control	7.40± 0.06	42.35± 0.35	14.85± 0.05	0.17± 0.014
Exhaust.	7.21± 0.23	40.75± 0.75	14.00± 0.40	1.55± 0.12
Exhaust.± Rec.	6.67± 0.52	37.45± 3.45	12.85± 1.05	7.23± 1.76
Without GINSENG :				
Control	7.38± 0.06	40.65± 0.95	14.40± 0.20	0.85± 0.007
Exhaust.	6.72± 0.22	35.75± 0.75	12.75± 0.15	1.4± 0.22
Exhaust.± Rec.	6.71± 0.12	35.00± 1.40	12.25± 0.95	1.53± 0.08

a similar pattern in the groups With and Without Ginseng, with a decrease of levels after the exhaustion exercise and after the recovery, although there were statistically non significant differences for the RBC in any case. The only remarkable difference for Hc and Hb values appears between the control group and the group after 48 h recovery Without Ginseng.

The presence of Reticulocytes is practically nonexistent in the control groups, being slightly higher - but not significantly - in the groups submitted to exhaustion exercise (stimulation and induction of reticulocytosis in the blood by intense muscular exercise) (Spodaryk et al. 1986), presenting higher statistically significant values only in animals treated With Ginseng after 48 h recovery, which reveals a slightly higher erythropoietic response in this group (Table 1).

Total Cholesterol levels show no difference between treatments nor as a consequence of exercise and recovery, except between the groups submitted to exhaustion exercise and 48 h recovery Without Ginseng (Fig. 2A). Triglycerides levels in plasma reveal, by comparing the control groups With and Without Ginseng, lower statistically significant values after the administration of Ginseng, in agreement with Bombardelli et al. (1980), Yokozawa et al.(1984) and Oura (1988), who indicate an increase in triglycerides levels as components of the adipose tissue and liver (lipogenesis in the liver and adipose tissue). Non - significant variations are obtained by comparing the values of the control groups whith those of the groups after exhaustion exercise and after 48 h recovery, both With and Without Ginseng (Fig. 2 B).

A light non - significant increase in urea levels is observed between the two control groups as a result of the Ginseng treatment, in agreement with Oura (1988). As expected, an urea level increase is observed after the exhaustion exercise, in concordance with lower protein levels, probably due to the relation between the protein catabolism and the ammonia elimination as urea. There are statistically significant differences between urea levels after exhaustion exercise and after recovery in the groups With and Without Ginseng (Fig. 3).

The results show that the groups treated with KRG present an increase of the glycogen stock in liver, which favours to get higher plasmatic glucose after exhaustive exercise than the ones

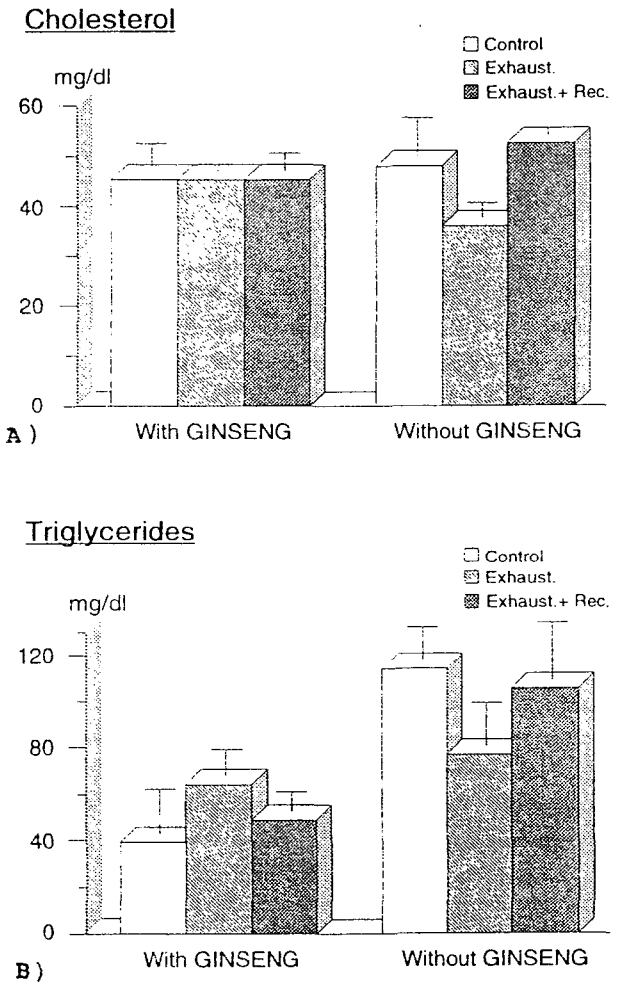
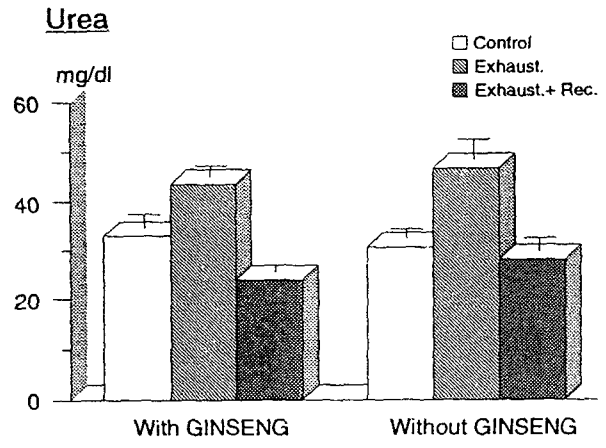
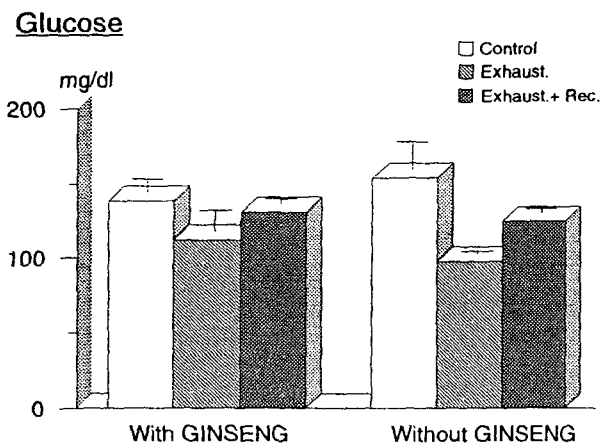
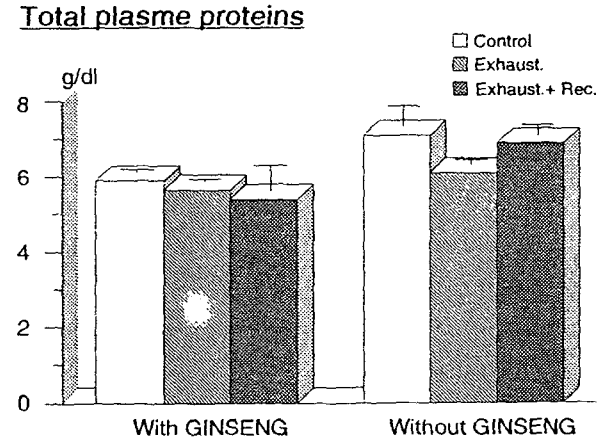


Fig. 2. Mean± SD plasma values of Total Cholesterol(A) and Triglycerides (B).

without KRG, even though they were running for about 30 more minutes. In addition, the hypoglucemic state was maintained significantly lower in rats treated without KRG after exhaustive exercise. After 48 h of recovery, the restitution of glycogen in liver, to reach resting - levels, is markedly better in groups treated with KRG, but this recovery doesn't appear so clearly in the experimental groups without Ginseng (Fig. 4).







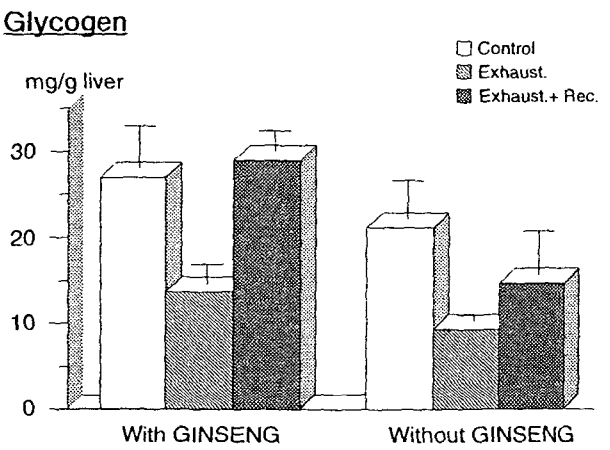


Fig. 3. Mean± SD plasma values of Urea and Total Proteins.

Fig. 4. Mean± SD values of plasma Glucose and liver Glycogen content.

Table corresponding to Fig. 2 and Fig. 3

	Cholesterol (mg/dl)	Triglycerides (mg/dl)	Urea (mg/dl)	Total protein (g/dl)
With Ginseng				
Control	45.5± 5.5	39.5± 19.5*	33.0± 2.8 *	5.9± 0.1*
Exhaust.	45.5± 1.5	64.5± 11.5	43.5± 2.1 *	5.7± 0.1
Exhaust.+Rec.	45.5± 3.5	49.0± 9.0*	24.0± 1.4	5.4± 0.7*
Without Ginseng				
Control	48.0± 8.0	114.5± 14.5	30.3± 2.1 *	7.1± 0.6 *
Exhaust.	36.0± 3.0 *	77.0± 19.0	46.5± 4.2 *	6.1± 0.1
Exhaust.+Rec.	52.5± 1.5	106.0± 25.5	28.0± 2.8	6.9± 0.3

* Statistical significant differences($p<0.05$) when each group of GINSENG is compared with the corresponding group without GINSENG.
* Statistical significant differences ($p<0.05$) between the different groups of each treatment

Table corresponding to Fig. 4

	Glucose (mg/dl)	Glycogen (mg/g liver)
With Ginseng		
Control	139.0± 9.0	27.0± 5.1
Exhaust.	112.5± 14.5	13.7± 2.3 *
Exhaust.+Rec.	131.5± 3.5	29.0± 2.5
Without Ginseng		
Control	154.0± 19.0 *	21.2± 4.6
Exhaust.	97.5± 1.5	9.3± 0.7
Exhaust.+Rec.	124.5± 3.5	14.8± 5.1

* Statistical significant differences($p<0.05$) when each group of GINSENG is compared with the corresponding group without GINSENG.
* Statistical significant differences ($p<0.05$) between the different groups of each treatment

Exhaustion exercise decreases significantly the muscle glycogen both in respiratory muscles and hindlimb muscles, with an evident supercompensation after 24 - 48 h recovery in respiratory muscles, and a recovery of the resting levels in the hindlimb muscles (Namiot and Gorski, 1988).

Plasmatic enzymes :

The study of plasmatic enzymes that can be indicators of tissue damage reveals a remarkable increase in the 48 h recovery post - exercise group Without Ginseng, in rapport to all the other groups, which proves the protective effect of the administration of KRG (Fig. 5).

The activity of LDH - indicator of specific muscular damage - in the 48 h recovery post - exercise group Without Ginseng, is statistically significant in rapport to all the rest of the groups With and Without Ginseng. Comparing the control groups,

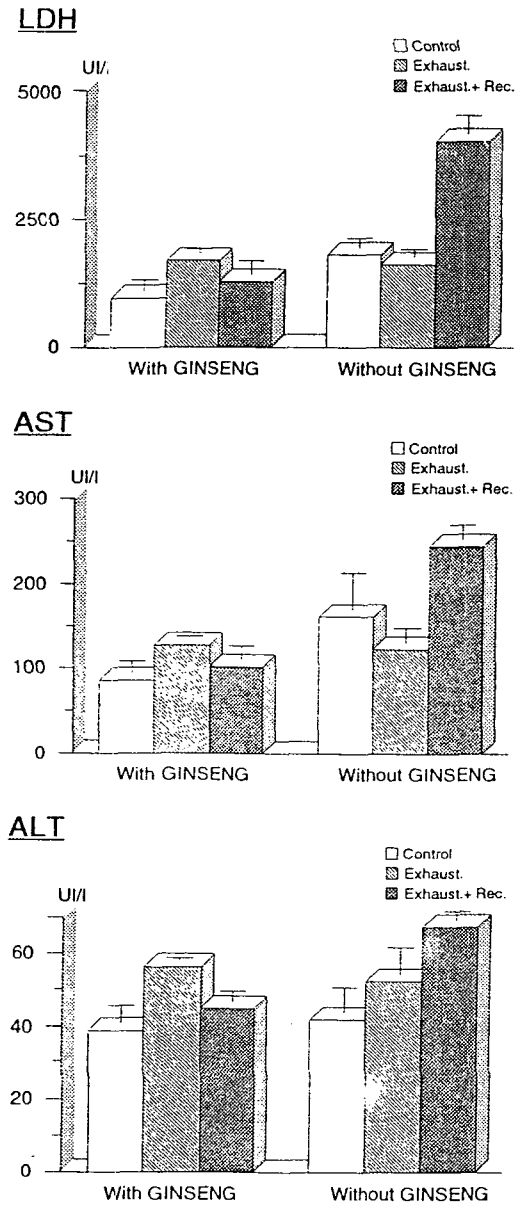


Fig. 5. Mean± SD values plasmatic enzymes indicators of possible tissular damage (LDH, AST and ALT).

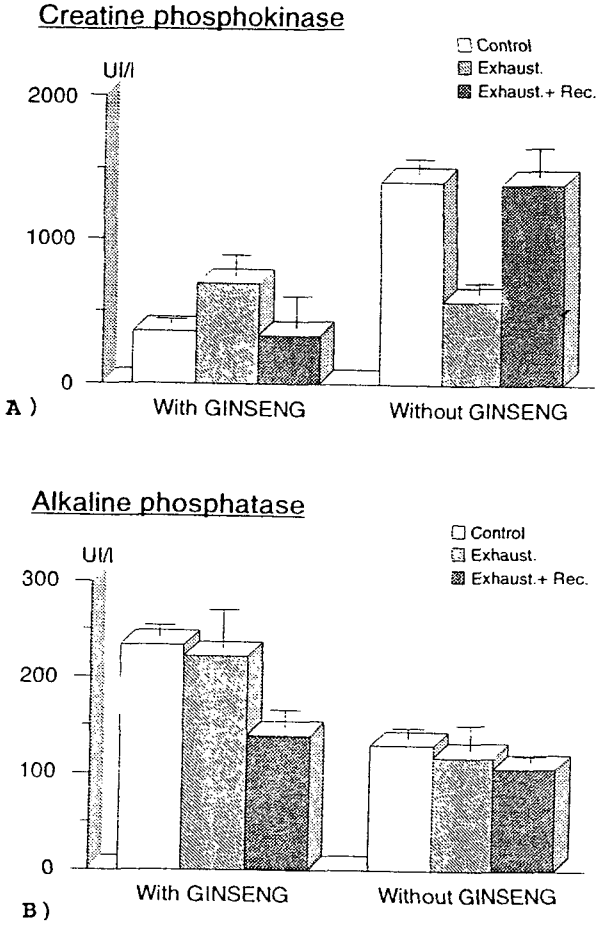


Fig. 6. Mean± SD values of plasma Creatine Phosphokinase (A) and Alkaline Phosphatase (B).

we also find statistically significant differences.

For the AST - indicator of possible hepatic, muscular or cardiac damage the activity level in the 48 h recovery post - exercise group Without Ginseng, is statistically significant in rapport to the values of the groups With and Without Ginseng. There are statistically significant differences between the levels of the control groups.

The ALT values - specific enzyme of hepatocytary functio-

Table corresponding to Fig. 5 and Fig. 6

	LDH (UI/l)	AST (UI/l)	ALT (UI/l)	Creatine Phosphokinase (UI/l)	Alkaline Phosphatase (UI/l)
With Ginseng					
Control	973.0± 227.0*	86.0± 14.0*	39.0± 5.0	360.5± 31.5*	233.5± 12.5
Exhaust.	1716.5± 93.5 *	127.5± 2.5	56.5± 0.5 *	693.0± 144.0	222.0± 41.0
Exhaust.+Rec.	1292.5± 285.5*	102.0± 17.0	45.0± 3.0*	334.0± 224.0*	139.5± 19.5
Without Ginseng					
Control	1824.5± 193.5	162.5± 43.5	42.0± 7.0	1412.5± 106.5	129.5± 10.5
Exhaust.	1624.5± 177.5* *	123.5± 17.5* *	52.5± 7.5*	579.0± 76.0	118.0± 25.0
Exhaust.+Rec.	4055.5± 366.5	248.0± 18.0	67.5± 2.5	1397.5± 200.5	106.5± 5.5

* Statistical significant differences($p<0.05$) when each group of GINSENG is compared with the corresponding group without GINSENG.

} * Statistical significant differences ($p<0.05$) between the different groups of each treatment

nality – show statistically significant differences in the 48 h recovery post – exercise group Without Ginseng, in rapport to the control groups and recovery group With Ginseng, but such differences don't appear between control groups. There is statistical difference between control and exhaustion group in treated with Ginseng.

The Creatin Phosphokinase – specific muscular enzyme whose levels increase sharply after 24 or 48 h of a muscular injury – doesn't experience such increase in the group With Ginseng, which indicates a KRG protection against the damage produced by exhaustion exercise (Fig. 6A).

Finally, the Alkaline Phosphatase presents an opposite tendency to the previous enzymes, probably due to the major importance of the bone regeneration in the groups treated With Ginseng (Fig. 6B).

Muscle enzymes :

The comparison of the LDH enzyme activity in rat and human muscle fibers in exhaustion exercise, shows a similar pattern with increased activity levels in the slow red, fast red and fast white fibers sequence. Such activity values in humans are slightly lower (Hintz et al. 1980).

The maximum activity of the LDH obtained by us after 48 h recovery, reflexes its catalitic action in the conversion between lactate and pyruvate in the muscle, specially in muscles with higher number of glycolitic cells (White Gastrocnemius), in agreement with Takekura & Yoshioka (1988) (Fig. 7).

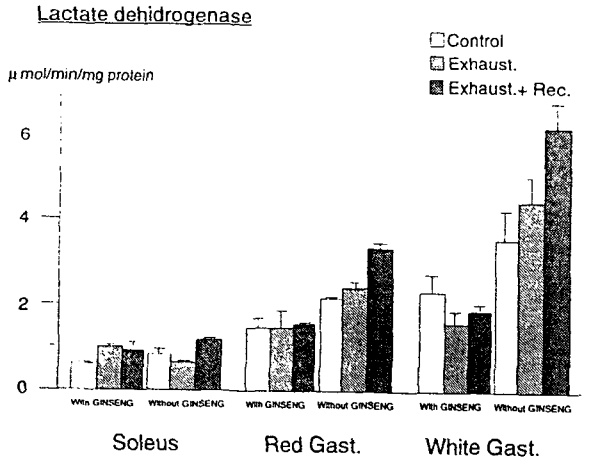


Fig. 7. Mean± SD values of LDH in Soleus, Red Gastrocnemius and White Gastrocnemius muscles.

Our results for the LDH activity in the muscular fraction studied, reveal that the activity is highest in the White Gastrocnemius in both groups : With and Without Ginseng. LDH activity levels in the Red Gastrocnemius are intermediate, with the lowest levels found in the Soleus.

In every case, the LDH activity values of groups Without Ginseng are higher than those of the groups treated with KRG, although significant differences can only be found in the case

Table corresponding to Fig. 7

	Lactate Dehidrogenase (μmol/min/mg protein)		
	Soleus	Red Gast.	White Gast.
With Ginseng			
Control	0.63± 0.03	1.48± 0.24*	2.35± 0.38
Exhaust.	1.62± 0.04*	1.44± 0.38*	1.60± 0.28
Exhaust.+Rec.	0.94± 0.18*	1.59± 0.01*	1.90± 0.14*
Without Ginseng			
Control	0.84± 0.14	2.18± 0.03	3.57± 0.65
Exhaust.	0.67± 0.05	2.44± 0.14	4.47± 0.57
Exhaust.+Rec.	1.20± 0.22	3.36± 0.14	6.25± 0.57

* Statistical significant differences($p<0.05$) when each group of GINSENG is compared with the corresponding group without GINSENG.
* Statistical significant differences ($p<0.05$) between the different groups of each treatment

of the White Gastrocnemius. Similar results were obtained by other authors such as Peter et al.(1971).

Our results can also be compared to those of the fore mentioned authors in the study of oxidative enzymes – Citrate Synthase (CS) in our study, and Succinate Dehydrogenase in Take-

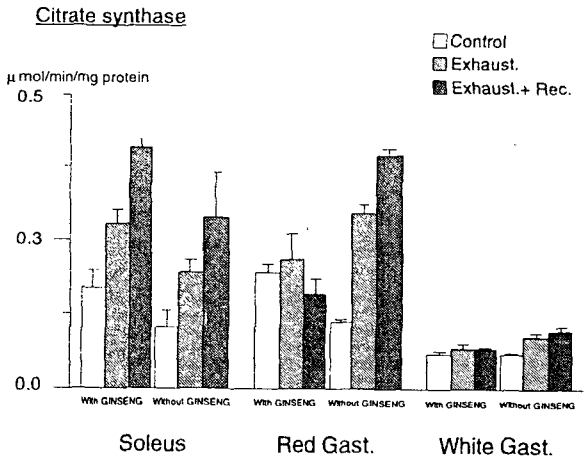


Fig. 8. Mean± SD values of CS in Soleus, Red Gastrocnemius and White Gastrocnemius muscles.

Table corresponding to Fig. 8

	Citrate Synthase (μmol/min/mg protein)		
	Soleus	Red Gast.	White Gast.
With Ginseng			
Control	0.170± 0.029	0.196± 0.013	0.060± 0.025
Exhaust.	0.279± 0.024	0.220± 0.042	0.070± 0.007
Exhaust.+Rec.	0.411± 0.015	0.161± 0.025*	0.070± 0.002*
Without Ginseng			
Control	0.103± 0.030	0.114± 0.005	0.060± 0.008
Exhaust.	0.197± 0.021	0.299± 0.014	0.090± 0.008
Exhaust.+Rec.	0.291± 0.077	0.400± 0.009	0.100± 0.008

* Statistical significant differences($p<0.05$) when each group of GINSENG is compared with the corresponding group without GINSENG.
* Statistical significant differences ($p<0.05$) between the different groups of each treatment

Fig. 3 The same two subpopulations of P.ginseng after 10th years of subcultivation. The period of the G_2 phase in mitotic cycle both subpopulations has increased.

kura & Yoshioka (1988) -. In the oxidative muscles, the activity of the CS increases with the exhaustion exercise and shows a maximum after 48 h of recovery. This situation is maintained in the Red Gastrocnemius, with far less evident changes in the White Gastrocnemius.

The Citrate Synthase (CS) - oxidative enzyme representing the citric acid cycle -, increases its activity with the exercise, especially in the red muscles. Its lowest activity is significant in the White Gastrocnemius, both With and Without Ginseng. Activity levels in the Red Gastrocnemius are intermediate but much closer to the activity levels in the Soleus, not existing statistically significant differences between them. There are no significant differences between With and Without Ginseng groups inside each muscle(Fig. 8).

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