

Original Article

Efficacy of Oral Korean Red-ginseng on sCRP and Soreness after Muscle Damage

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Objectives : The study investigated the efficacy of oral Korean red-ginseng (RG) on sCRP response mediated by eccentric contraction-induced muscle damage and discussed its mechanism.

Methods : Nineteen healthy young subjects (aged 24.4 ± 2.07 yr) volunteered for this double blind test. They were classified into either the RG group (N=10) or placebo (P) group (N=9) during the 10-d experimental protocol. Blood samples were collected on T1 (baseline), T1 (1h), T2 (1d), T3 (2d) and T4 (3d) after eccentric contraction-induced injury on the seventh day. Statistical analyses were conducted using nonparametric methods ($p < 0.05$).

Results : The RG group increased sCRP more than P group and didn't increase soreness peak at T2, not significant. There were no correlations between soreness intensity and sCRP. Oral RG had little efficacy for reducing sCRP at the muscle damage-mediated acute phase; rather, it increased because of its proinflammatory cytokine production.

Conclusions : Oral RG could stimulate proinflammatory cytokine production, and occasionally bal-pyo-beob could be helpful for the efficient recovery of muscle injury.

Key Words: Korean red-ginseng, Muscle damage, sCRP, soreness, bal-pyo-beob

Introduction

Korean ginseng (*Panax ginseng* C. A. Meyer) is known as a potent adaptogen against infection and stress.^{1,2} Korean red-ginseng (RG) is one of its primary processed products. Both of them have similar efficacies; additionally, RG is anti-thrombotic.³ The typical contraindication of oral ginseng is sil-yeol syndrome (實熱證).⁴ So the clinical case of either treatment of heo-yeol syndrome (虛熱證) or the

resultant complaint of fever by their usage has often confused at the diagnosis itself if wrong or not. Eccentric muscle contraction (EC) induces indirect muscle damage,⁵⁻⁷ DOMS (delayed onset muscle soreness),⁸ edema⁹ and increase of plasma muscular proteins;¹⁰ i.e. creatine kinase (CK), etc. These are similar to inflammation-induced symptoms, and DOMS would be mediated by inflammation.⁸ Especially, the serum C-reactive protein (sCRP) level is responded dramatically in blood on an acute muscle contraction.¹¹

Ginseng has been known to elevate physical and psychophysical performances.¹² How does oral RG affect the experimental muscle damage-mediated inflammation responses induced by EC? So, the main objective of this study was the measurements of sCRP

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Table 1. 1. Main Ingredients of Placebo and Red-ginseng Treatments.

Ingredients†(per 100ml)	Treatments	
	Placebo (P)	Red-ginseng (RG)
Red-ginseng Extract (g)	0	6.0*
<i>Agastachis Herba</i> (g)	≤ 4.0**	≤ 0.5

*, Dry red-ginseng (RG) 12g with water plus 70% fermented alcohol was concentrated six times into RG solidity-extract >70%.

**, *Agastachis Herba* 4.0g with its water content 15% was boiled with water at 120°C for 120 minutes and made into 100ml water-extract.

and subjective perceived muscle soreness scales, and the observation of pain pattern of lower extremities. And then, the purpose is to investigate the efficacy of oral RG in the acute phase compared with P (placebo), under the condition of controlling CK peak levels of two groups as moderate response (500 ~2000 U/l)¹³ after eccentric muscle contraction.

Methods

Healthy 24.4 ± 2.07 year old male subjects (N=19)

were classified as red-ginseng group (N=10) and placebo group (N=9). This random classification didn't affect BL comparison between the two groups in age, height, HR and BP. Differences between the two groups in sCRP (mean ± SE; 0.04 ± 0.01 vs 0.05 ± 0.01 mg · dl⁻¹) were not significant at baseline (BL) (*F*-test; *p*=0.09). The treatment-materials were represented as <Table 1>, and the experimental design for the double-blind test (Figure 1). Experimental muscle damage protocol was adapted -7°C downhill running for 60 min at the speed of 12km · h⁻¹, including rest time 5 min in the middle of running. Oral P or RG twice a day for 10 days, performed downhill running on the 7th day. Blood was taken from the antecubital vein at BL (T1), T1' (1h), T2 (1d), T3 (2d) and T4 (3d after eccentric contraction) and treated by heparin. The blood aliquots were then centrifugated at 1500 × g for 5 min. Plasma was were stored immediately at -70°C before assessment. And sCRP was measured using enzyme-linked immunosorbent assay system at Clinical Laboratory in Green Cross Institute. The scaling pain was measured at T1', T2, T3 and T4 using scaling remodelled from 0 ~6

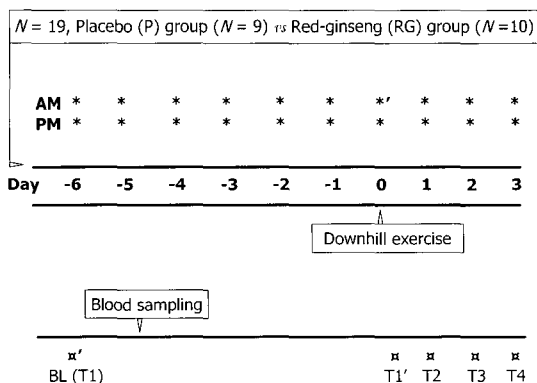


Fig. 1. Experimental design for the efficacy test of oral red-ginseng on muscle damage-mediated acute phase response. *, Each 100ml of placebo (P) or red-ginseng (RG) was administrated in the morning and afternoon. α, P or RG in the morning on downhill running (eccentric contraction) was additionally with water 110ml. α', blood sampling at BL (T1), α, blood sampling at T1' (1h), T2 (1d), T3 (2d), T4 (3d after downhill running).

Table 2. Scaling Muscle Soreness.

Grade	Complaint
0	Not at all or little painful by touch
1	A little painful by touch, its continued
2	Also maybe a little painful on motion
3	A little painful on motion
4	Painful or stiff only on motion
5	Painful or stiff on motion or walking, its continued
6	Painful or stiff enough for limitation of ROM

modified Likert scale of muscle soreness¹³⁾ <Table 2>.

Data were recorded as mean \pm SE. Equality of variance assumptions were examined by an F-test. If significant deviation from deviation from these assumptions was observed, nonparametric methods were employed; otherwise, continuous variables were analyzed with a nonpaired *t*-test. Comparisons between groups for changes in outcome efficacy measures post-versus pre-downhill running were analyzed by the Mann-Whitney U-test, correlation by Pearson's.

Results

All subjects' sCRP levels were within normal range (≤ 0.20 mg/dl)¹⁴⁾ at BL. The difference between deviations of the two groups was not significant in sCRP response (F-test; $p=0.09$) (Figure 2).

Both of two groups, were increased in sCRP at T2 (P group, 0.05 ± 0.01 mg/dl vs RG group, 0.12 ± 0.07 mg/dl) more than at T1 (P group, 0.04 ± 0.01 mg/dl vs RG group, 0.05 ± 0.01 mg/dl), not significantly between them either (F-test, *t*-test; $p>0.05$) (Figure 2 & 3). Each was recovered at T3 (P group, 0.04 ± 0.00 or at T4 (RG group, 0.05 ± 0.01 mg/dl). Differences between the two groups in T2-T1, T3-T1 and T3-T2 were not significant (Mann-Whitney U-test; $p>0.05$) (Figure 4). And sCRP level at T2 in RG group had correlated with T1 more than in P group. (P group, $r=0.62$ vs RG group, $r=0.81$). DOMS was most severe at T2 (P group, 5.2 ± 0.3 grade vs RG group, 4.7 ± 0.5 grade) than at other time points, being P group more than RG group (Figure 5). And both were recovered almost at T4. Muscle soreness occurred mainly around femoralis rectus (Figure 6).

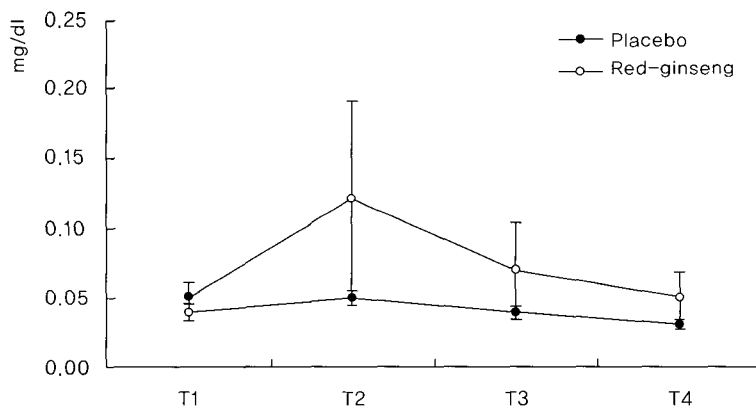


Fig. 2. Serum C-reactive protein (sCRP) response before and after eccentric contraction-induced muscle damage. At baseline (T1), and 1day (T2), 2day (T3) and 3day (T4) after downhill-exercise, sCRP (mg/dl⁻¹) of red-ginseng group (N=10; O) and placebo group (N=9; ●) were assessed. There were no significant differences in sCRP levels between two groups (F-test, *t*-test; $p>0.05$).

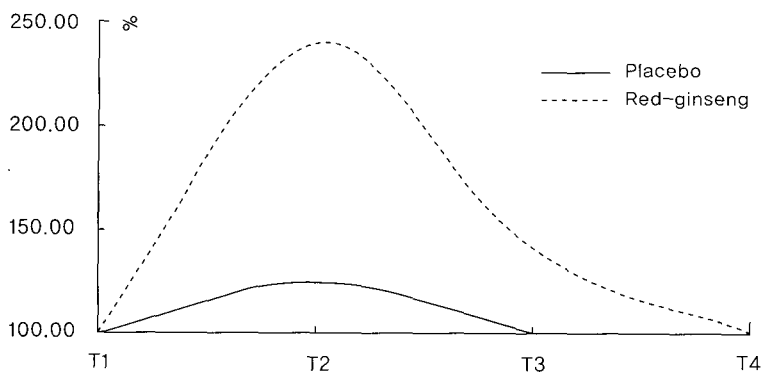


Fig. 3. The change rate of serum C-reactive protein (sCRP) levels after eccentric contraction-induced muscle damage. Compared with baseline (T1), the change rate of sCRP (mg/dl) of red-ginseng group (N=10; dot line) and placebo group (N=9; straight line) at 1day (T2), 2day (T3) and 3day (T4) after downhill-exercise were assessed. There were no significant differences in sCRP levels between two groups (F-test, t-test; $p>0.05$).

Discussion

Each peak level of sCRP in the P group and the RG group was presented at T2, each around 120% and 240% increased than T1. The P group was recovered at T3 and the RG at T4. There were both peak levels of sCRP and CK at the third day after eccentric contraction of upper extremity.¹⁵⁾ We controlled the CK peak levels (P group, 625.01 ± 225.23 U/l vs RG group, 774.50

± 129.82 u/l⁻¹) at T2 (figure not shown) for the purpose of maintaining less danger for the subjects' safety. DOMS intensity of the P group was stronger than the RG group. It doesn't indicate that the higher sCRP, the more soreness. There were no data about sCRP immediately after oral RG for 6 days in this study. However, it was assumed that oral RG could increase sCRP at rest, because matters to stimulate innate immunity in RG induce production of

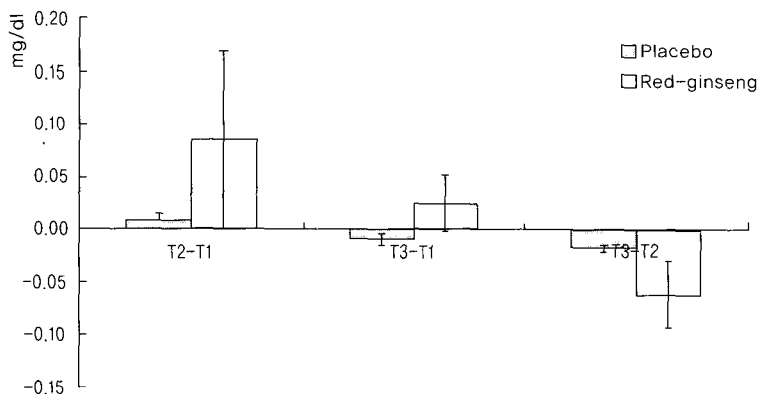


Fig. 4. Differences of serum C-reactive protein (sCRP) between time points. Differences of sCRP levels (mg/dl) of red-ginseng group (N=10; □) and placebo group (N=9; ▒) were assessed; i.e. T2-T1, T3-T1 and T3-T2. There were no significant differences in sCRP levels between two groups (Mann-Whitney U-test; $p>0.05$).

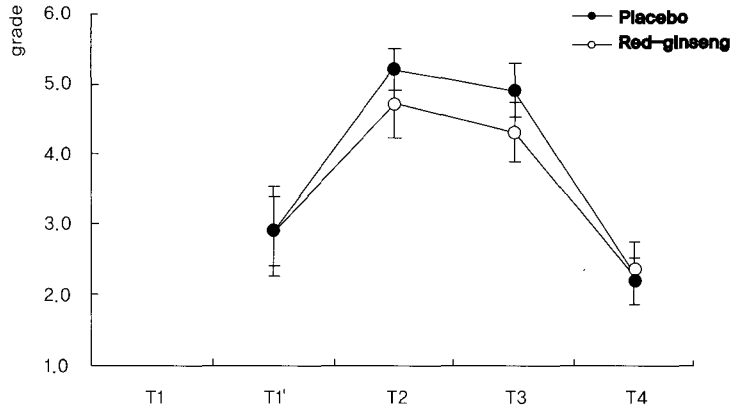


Fig. 5. Scaling of Muscle Soreness. Pain grades of placebo group (N=9; ●) and red-ginseng group (N=10; ○) were measured at T1' (1h), T2 (1d), T3 (2d) and T4 (3d after downhill running). Differences within and between two groups were not significant (*t*-test; $p>0.05$).

proinflammatory cytokines through toll-like receptors in pancreatic cells.¹⁶ The activity of IL-6 among them reflects the sCRP synthesis capacity;¹⁰ the level of sCRP almost isn't affected by its secretory circadian rhythm.¹⁷ The $t_{1/2}$ of sCRP depends on its synthetic rate, and then healing inflammation and/or tissue destruction decreases sCRP level fast within 4 ~9 hours.¹⁸ There were no significant differences between groups in T5-T2, T3-T2, T4-T2, T6-T2 and T6-T5

(Mann-Whitney U-test; $P>0.05$).

Muscle soreness occurred nearly on *jog-yang-myeong-wee-kyeong* (足陽明胃經) around femoralis rectus bilaterally. There were no correlations between soreness intensity and sCRP. Among tetracyclic triterpenoid saponin glycosides in RG, Rg1 increases blood pressure and stimulates CNS and Rb1 does reversely.¹⁹ We didn't measure the contents of Rg1 and Rb1 in the material. After this 10-day experimentation,

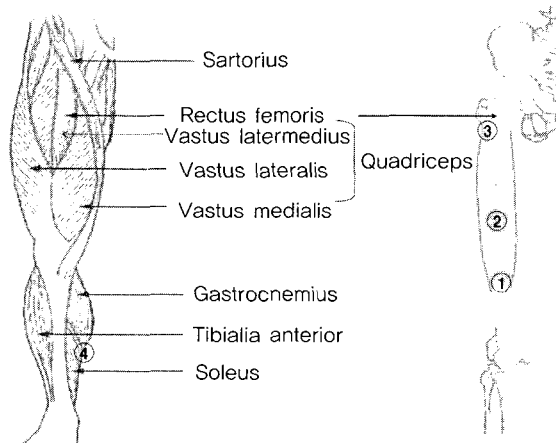


Fig. 6. Eccentric contraction-induced muscle soreness (A-P view in right extremity). ① and ③, the proximal and distal muscle-tendon junctions of rectus femoris (RF). ②, the upper layer of RF, convex part above quadriceps. ④, soleus-archilles tendon.

three subjects in the RG group emphasized their revitalization; there was one instant insomnia among them, who then required oral RG sustained. Because both of sCRP levels at T2 didn't represent chronic inflammatory pathology, DOMS seemed to be mechanical hyperalgesia including inflammatory pain. Hyperalgesia is caused by hyper-sensitivity of nociceptors by innate mediators.²⁰⁾ Now we suggested that oral RG stimulates CNS, and then the efficient blood flow to fatigued muscles. Consequently, oral RG seemed dedicated to treatment of local ischemia and/or removal of pain-related matters. It is necessary to use both as ginseng and bal-pyo-je (發表劑) for *ki-heo yang-heo* (氣虛·陽虛), because only it could make inflammatory symptoms worse.⁴⁾ Strictly speaking, this study showed that oral RG had little efficacy for reducing sCRP at the muscle damage-mediated acute phase. However, we found that oral RG could stimulate proinflammatory cytokine production, and occasionally bal-pyo-beob (發表法) could be applied to muscle injury treatment.

Conclusion

Oral RG had little efficacy for reducing sCRP at muscle damage-mediated acute phase; rather, it increased because of its proinflammatory cytokine production. Occasionally, bal-pyo-beob (發表法) could be helpful for the efficient recovery of muscle injury.

References

1. Bahrke MS & Morgan WP. Evaluation of the ergogenic properties of ginseng. *Sports Medicine*. 2000;29:113-133.
2. Roman A & Houston P. Herbal products: ginseng. *Pharmaceutical Journal*. 1995;255:150-152.

3. Oh SJ, Park IH & Kim SH. Effects of Prescription including Korean Red-ginseng on Experimental Cerebral Infarction; *Journal of KOMS*, 1999;20:161-171.
4. Lee SI, Ahn DG, Shin MK, Noh SH, Lee YJ, Kim SH. *Clinical Application of Herbs*. Seoul, Seongbosa. 1982.
5. Best TM & Hunter KD. Muscle injury and repair. *Physical Medicine and Rehabilitation Clinics of North America*. 2000;11:251-266.
6. Dugan SA & Frontera WR. Muscle fatigue and Muscle injury. *Physical Medicine and Rehabilitation Clinics of North America*. 2000;11:385-403.
7. Proske U & Morgan DL. Muscle damage from eccentric exercise: mechanism, mechanical signs, adaptation and clinical applications. *The Journal of Physiology*. 2001;537:333-345.
8. Clarkson PM & Hubal MJ. Exercise-induced muscle damage in humans. *American Journal of Physical Medicine and Rehabilitation*. 2002;81:S52-S69.
9. Friden J & Lieber RL. Eccentric exercise-induced injuries to contractile and cytoskeletal muscle fibre components. *Acta Physiologica Scandinavica*. 2001;171:321-326.
10. Herity NA. Interleukin-6: a message from the heart (Editorial). *Heart*. 2000;84:9-10.
11. Gabay C & Kushner I. Acute-phase proteins and other systemic responses to inflammation. *New England Journal of Medicine*. 1999;340:448-454.
12. Clarkson PM, Nosaka K & Braun B. Muscle function after exercise-induced muscle damage and rapid adaption. *Medicine & Science in Sports & Exercise*. 1992;24:512-520.
13. Slater H, Arendt-Nielsen L, Wright A & Graven-Nielsen T. Experimental deep tissue pain in wrist extensors - a model of lateral epicondylalgia.

- European Journal of Pain. 2002;7:277-288.
14. Ballou SP & Kushner I. C-reactive protein and the acute phase response. *Advances in Internal Medicine*. 1992;37:316-336.
 15. Phillip T, Childs AC, Dreon DM, Phinney S & Leeuwenburgh C. A dietary supplement attenuates IL-6 and CRP after eccentric exercise in untrained males. *Medicine & Science in Sports & Exercise*. 2003;35:2032-2037.
 16. Nakaya TA, Kia M, Kuriyama H, Iwakura Y & Imanishi J. Panax ginseng induces production of proinflammatory cytokines via toll-like receptor. *Journal of Interferon & Cytokine Research : the Official Journal of Interferon & Cytokine Research*. 2004;24:93-100.
 17. Meier-Ewert HK, Ridker PM, Rifai N, Price N, Dinges DF & Mullington, JM. Absence of diurnal variation of c-reactive protein concentrations in healthy human subjects. *Clinical Chemistry*. 2001;47:426-430.
 18. Young B, Gleeson M & Cripps AW. C-reactive protein: a critical review. *Pathology*. 1991;23:118-124.
 19. Roman A & Houston P. Herbal products: ginseng. *Pharmaceutical Journal*. 1995;255:150-152.
 20. Mense S & Meyer H. Bradykinin-induced modulation of the response behaviour of different types of feline group and muscle receptors. *The Journal of Physiology (London)*. 1998;398:49-63.