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Original Article

Anti-fatigue effects of Radix Astragali in plateau humans

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Abstract: To evaluate the physical performance of adult human in the plateau, and to explore the anti-fatigue effects of Radix Astragali. 40 human males were selected who had acclimatized to 3700-m altitude. Divided the subjects into two groups randomly (n=20): One is control group, the other is Radix Astragali group. According to military standard GJB1337-92, the physical work capacity (PWC170), VO_2max, and step test index was measured before and after taking Radix Astragali. Venous blood was sampled to detect the level of blood lactic acid (BLA), blood urea nitrogen (BUN), superoxide dismutase (SOD) and 3,4-Methylenedioxyamphetamine (MDA). Compared with control, the Radix Astragali increased PWC_{170}, step test index and SOD, and reduced the heart rate, BLA, BUN and MDA in the after-exercise group. These results demonstrate that Radix Astragali may be a new therapy for fatigue caused by plateau-condition hypoxia.

Keywords: Fatigue, plateau, Radix Astragali, blood lactic acid (BLA), superoxide dismutase (SOD)

Introduction

Fatigue includes physical fatigue and mental fatigue. Physical fatigue is that people cannot continue to work under the given labor intensity [1, 2]. Several theories explain physical fatigue, such as clogging theory, exhaustion theory and radical theory [3, 4]. Rapid ascent to a high altitude environment decreases the working performance of sea level residents, and is a general phenomenon of poor acclimatization to hypoxia. Search for medicine to strengthen anti-fatigue capability and quickly restore physical strength and energy is crucial. Scholars have found some anti-fatigue drugs under plain environment, including salidroside from *Rhodiola rosea* [5], eleutheroside from *Acanthopanax senticosus* [6], crocetin [7], etc. Rhodiola rosea showed the anti-fatigue effects by using a weight-loaded swimming test on mice, and the anti-fatigue mechanisms of it were evaluated by using metabolomics on multiple targets in vivo [5]. Acanthopanax senticosus is mainly added by increasing the use of fat, delaying the increase of blood urea nitrogen (BUN), and reducing the accumulation of lactic acid can act as an anti-fatigue action [6]. Daily administration of crocetin may attenuate physical fatigue in men [7]. However, drugs for anti-fatigue are still not used widely in human under the plateau environment.

Radix Astragali as a traditional Chinese medicine has been used to treat some disease [8]. This substance is considered to exhibit anticancer [9], and anti-diabetes properties [10], to improve immunity [11], and to regulate the cardiovascular and urinary systems [12]. The major biologically active components of Radix Astragali are astragaloside, astragalus polysaccharide, aminobutyric acid and some microelement selenium. Radix Astragali was eliminated linearly in rats [13, 14]. Distribution of Radix Astragali in tissue showed that the substance was widely distributed in vivo [15]. The Radix Astragali is distributed in the lung, liver, skin, kidney, gastrointestinal tract and heart in rats [15].

Radix Astragali could alleviate physical fatigue in humans and animals under a normoxic environment [16, 17]. Myelophil appears to have a

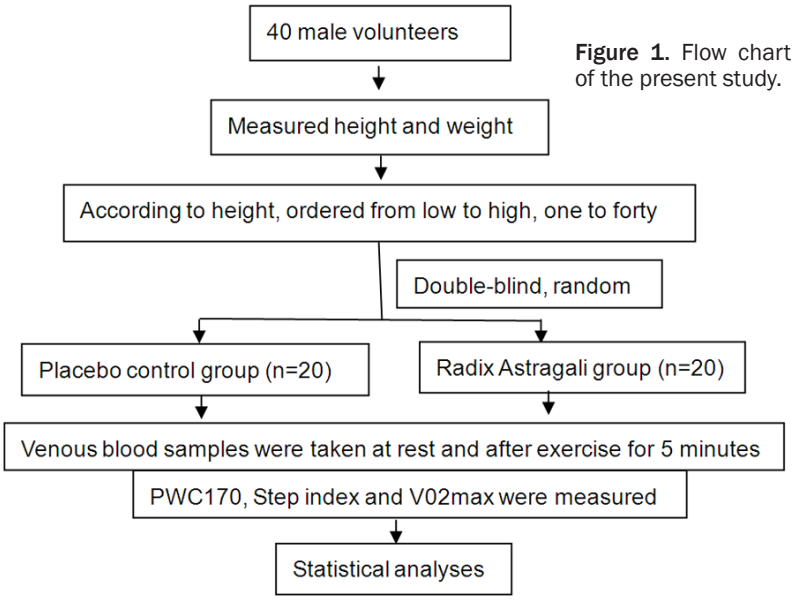

Figure 1. Flow chart of the present study.

Table 1. Characteristics of the subjects

	Control group	Radix Astragali group
Ages (years)	20.87±1.73	20.00±1.41
Height (cm)	175.75±1.83	175.00±2.00
Weight (kg)	66.13±2.03	65.75±1.98

The values are expressed as the mean ± SD.

pharmacological effect against fatigue, suggesting the clinical relevance of the traditional medicinal plants, Astragalus membranaceus and Salvia [16]. Astragalus membranaceus flavonoids could significantly counteract the aberrant cytokine production, then to exhibit a higher endurance capacity to swim in rats [17]. Previous studies have found that Radix Astragali can alleviate physical fatigue in simulated plateau-condition mice [18], whereas the anti-fatigue effects of Radix Astragali in plateau humans are not well understood.

The current research was designed to ascertain the anti-fatigue property of Radix Astragali in the plateau humans by determining the physical work capacity (PWC_{170}), VO_2max, blood lactic acid (BLA), blood urea nitrogen (BUN), superoxide dismutase (SOD) and 3,4-Methylenedioxyamphetamine (MDA) in humans.

Materials and methods

Design

The design of the present study was shown in **Figure 1**.

Subjects

Forty healthy male volunteers, who had acclimatized to 3700-m altitude, were divided into two groups randomly (n=20): One is control group, the other is Radix Astragali group; the basic information of two groups is shown in **Table 1**. The double-blind principle was used in this randomized case-control study.

Drugs

Radix Astragali tablets were purchased from the Sichuan Guokang pharmaceutical industry limited company (country medicine accurate character Z20090761). Each tablet contains 0.5 grams of Radix Astragali, and four tablets were taken each time, twice a day for 15 continuous days. The control group received placebos, which contained 0.5 grams of flour. The placebo was administered in the same dose and amount as the Radix Astragali. All the test indexes were measured before and after the subjects took the medicine.

PWC_{170} test

PWC170 represents the amount of work per unit time (kg·m/min) when the heart rate reaches 170 b/min. Physical fitness for soldiers was measured, according to the national military standard method. Fitness was evaluated using a two-stage quantitative load step motion experiment. First-stage quantitative load step is 40 centimeters high, and the subjects went up the step at the speed of 24 step/min for 5 mins. The second-stage quantitative load step test required subjects to step at a speed of 25 step/min for 5 mins. Power and PWC_{170} [19, 20] were calculated according to the following formula:

Power (kg·m/min)=4/3 [Body weight (kg) × step height (m) × frequency of up and down the step (b/min)]

PWC_{170} (kg·m/min)=N_1 + (N_2-N_1) × [(170-f_1)/(f_2-f_1)]

Table 2. Effects of Radix astragali extracts on HR after exercise at altitude of 3700 m

	Control group	Radix astragali group	P
HR at rest			
Before taking medicine	82.00±10.92	84.73±8.57	
After taking medicine	86.86±6.36	78.13±8.08[c]	P_c=0.036
HR at first peak[#]			
Before taking medicine	160.07±11.19	160.80±12.90	
After taking medicine	161.20±14.85	147.33±10.46[b,c]	P_b=0.008 P_c=0.050
HR at second peak[#]			
Before taking medicine	169.20±10.43	170.73±13.28	
After taking medicine	178.67±13.91	158.13±10.81[a,d]	P_a=0.029 P_d=0.005

Abbreviations: HR, heart rate. [#]First peak means after the first-stage quantitative load step. Frst-stage quantitative load step is 40 centimeters high, and the subjects went up the step at the speed of 24 step/min for 5 mins. The second peak means after the second-stage quantitative load step. The second-stage quantitative load step test required subjects to step at a speed of 25 step/min for 5 mins. The HR was measured at rest, at first peak, at second peak, respectively. [a]*P*<0.05, [b]*P*<0.01, compared to before taking medicine; [c]*P*<0.05, [d]*P*<0.01, compared to control group (n=20).

Table 3. Effects of Radix astragali extracts on SaO_2 after exercise at altitude of 3700 m

	Control group	Radix astragali group
SaO_2 at rest		
Before taking medicine	91.00±1.85	91.00±2.62
After taking medicine	91.20±1.78	90.53±1.73
SaO_2 after exercise		
Before taking medicine	87.93±3.15	86.00±3.42
After taking medicine	88.13±3.29	87.80±2.57

Abbreviations: SaO_2, arterial O_2 saturation.

N_1 and N_2 represent the power of the first and the second-stage quantitative load, respectively. f_1 and f_2 represent the heart rate associated with N_1 and N_2, respectively.

Step index test

According to military standard GJB1337-92, the step is 40 centimeters high, and the subjects went up the step at the speed of 30 steps per minute, 5 minutes of exercise. The subjects stand before the step after the exercise, and the heart rate is tested at 1-1.5, 2-2.5, and 4-4.5 min. Then, calculate the step index according to the following formula:

Step index=300 sec (exercise time)/2 [(1~1.5 + 2~2.5 + 4~4.5) min heart rate] × 100

Maximal oxygen consumption (VO_2max) test

According to military standard GJB1337-92, the VO_2max was calculated according to the following formula:

VO_2max=(1.2186 + 0.01984W + 0.07259VC-0.006659MP) × 1000/W

VC, MP and W represent vital capacity, morning pulse (unit: b/min), and body weight (unit: kg), respectively.

Blood biochemical assays

Venous blood samples were taken at rest and before or after taking medicine after exercise for 5 minutes. The content of BLA, BUN, SOD and MDA was measured according to the assay kit's instructions. The assay kits were purchased from Jiancheng Bioengineering Institute (Nanjing, China).

Statistical analyses

Using SPSS18.0 version performed statistical analyses (SPSS Inc., Chicago, USA). The indicators were compared in two ways, one was the Radix Astragali group compared to the placebo group, and the other was after taking medicine compared to before taking medicine. In addition, in blood biochemical assays, a one-way analysis of variance (ANOVA) was used to analyze the differences among different time points. All the test indexes were analyzed by the following statistical methods. The differences between control groups and Radix Astragali groups were analyses by Independent-Sample T Test. The differences between before and after taking medicine groups were analyses by Paired-Sample T Test. The data were expressed as mean ± S.D. The significance was set at P<0.05.

Results

Effects of radix astragali on heart rate (HR) and arterial O_2 saturation (SaO_2)

As shown in **Table 2**, compared to before taking medicine, taken Radix Astragali for 15 days significantly decreased the HR at first peak and

Table 4. Effects of Radix astragali extracts on VO_2max, PWC_{170} and step index test at altitude of 3700 m

	Control group	*Radix astragali* group	P
VO_2max (ml/kg/min)			
Before taking medicine	41.01±2.83	40.85±3.31	
After taking medicine	40.93±3.69	44.25±2.82[b]	P_b=0.006
PWC_{170} (kg·m/min)			
Before taking medicine	882.25±120.07	870.83±105.98	
After taking medicine	737.86±137.68[a]	992.58±108.71[d]	P_a=0.024 P_d=0.001
Step index test			
Before taking medicine	96.49±11.68	96.34±11.08	
After taking medicine	96.60±6.88	109.15±13.65[c]	P_c=0.036

Abbreviations: VO_2max, Maximal oxygen consumption; PWC_{170}, physical work capacity. [a]*P*<0.05, [b]*P*<0.01, compared to before taking medicine; [c]*P*<0.05, [d]*P*<0.01, compared to control group (n=20).

the second peak. First peak means after the first-stage quantitative load step, and the second peak means after the second-stage quantitative load step. Compared to control group, taken Radix Astragali significantly decreased the HR at first peak and the second peak. Control group showed no difference before and after taking the medicine. The Radix Astragali did not significantly affect the SaO_2 after exercise (**Table 3**).

Effects of radix astragali on exercise ability (VO_2max, PWC_{170}, step index test)

The results shown in **Table 4** represent the effects of Radix Astragali on the exercise ability of humans. Compared to before taking medicine, Radix Astragali significantly increased the VO_2max, whereas PWC170 was significantly decreased in control group. Compared to control group, Radix Astragali significantly increased the PWC_{170} and step test index.

Effects of radix astragali on blood biochemical indexes (include BLA, BUN, SOD and MDA)

The effects of Radix Astragali extract on BLA, BUN, SOD and MDA as shown in **Table 5**. Compared to the condition of rest, the BLA, BUN and MDA were significantly increased in the after-exercise group, whereas SOD was significantly decreased. In the Radix Astragali group, compared to before taking medicine, Radix Astragali significantly decreased BLA, BUN and MDA. Compared to the control group, taking Radix Astragali significantly decreased the BLA, BUN and MDA, and increased SOD after exercise.

Discussion

In this study, we investigated the anti-fatigue effect of Radix Astragali in plateau-condition humans. Exercise ability of humans can be demonstrated by the PWC_{170}, step index test and VO_2max. PWC170 is a common index to evaluate the ability to perform manual labor. The step index test is a simple method to evaluate the function of the cardiovascular system by testing the quantified load movement. The VO_2max represents the amount of oxygen a person can take in for one min under the maximum cardiovascular function. In the present study, Radix Astragali was able to significantly increase the VO_2max, PWC_{170} and step test index, suggesting that Radix Astragali can evaluate the ability to perform manual labor in plateau-condition humans.

Lactic acid is a metabolic product of the anaerobic glycolysis, strong physical exercise will cause a lot of lactic acid in the muscles, especially in the high altitude hypoxia environment. Therefore, lactic acid can be used as an index to evaluate the fatigue state and the elimination of fatigue [21-23]. Accordingly, the redundant lactic acid induces many side effects that are harmful to the body performance and that cause fatigue. In our study, Radix Astragali produced a significant effect to reduce the BLA level in humans.

The BUN is a conventional parameter for evaluating the metabolic catabolism of protein during exercise. In a physiologic condition, the state between generation and excretion of BUN represents an equilibrium. In an exhaustive condition, protein catabolism provides energy, which results in an increase of BUN [24]. In addition, nucleotide metabolism can be reinforced by movement. Nucleotide metabolism removes an amino group, which can generate urea through the urea cycle, and urea is a participant in generating BUN. In this study, taking Radix Astragali significantly decreased BUN, indicating that Radix Astragali can accelerate the elimination of BUN, thus maintaining the

Table 5. Effects of Radix astragali extracts on blood biochemical indexes at altitude of 3700 m

	Control group	Radix astragali group	P
BLA			
At rest	3.00±1.25	2.84±0.75	
Before take medicine + after exercise	5.39±2.87	4.08±0.91[b]	P_b=0.002
Take medicine + after exercise	6.42±3.83[a]	3.27±0.80[c,e]	P_a=0.012 P_c=0.014 P_e=0.02
BUN			
At rest	5.39±1.90	4.65±1.43	
Before take medicine + after exercise	9.03±3.04[b]	7.40±1.88[b]	$P_{b\ (control)}$=0.009 $P_{b\ (RA)}$=0.001
Take medicine + after exercise	9.16±3.50[b]	6.04±1.43[a,c,e]	P_b=0.007 P_c=0.050 P_e=0.018
SOD			
At rest	93.28±13.87	93.75±9.75	
Before take medicine + after exercise	77.48±10.41[b]	80.58±5.40[b]	$P_{b\ (control)}$=0.010 $P_{b\ (RA)}$=0.004
Take medicine + after exercise	73.22±13.45[b,c]	87.18±11.85[e]	P_b=0.001 P_c=0.030 P_e=0.024
MDA			
At rest	5.22±1.93	4.70±1.22	
Before take medicine + after exercise	9.03±3.85[a]	9.05±3.69[b]	P_a=0.018 P_b=0.000
Take medicine + after exercise	9.59±3.99[b]	5.78±1.21[c,f]	P_b=0.008 P_c=0.044 P_f=0.010

Abbreviations: BLA, blood lactic acid; BUN, blood urea nitrogen; SOD, superoxide dismutase; MDA, 3,4-Methylenedioxyamphetamine. [a]*P*<0.05, [b]*P*<0.01, compared to at rest state; [c]*P*<0.05, [d]*P*<0.01, compared to before take medicine + after exercise group; [e]*P*<0.05, [f]*P*<0.01, compared to control group.

balance of BUN and enhancing resilience to exercise.

During hypoxia, there was an increase in the production of free radical. The free radical content can be increased by cell anoxia with a decrease in SOD activity and an increase in MDA [25, 26]. Therefore, SOD and MDA levels can reflect the degree of hypoxia. In this study, taking Radix Astragali significantly increased SOD, and significantly decreased MDA, indicating that Radix Astragali can promote the balance of oxidation and antioxidant to exercise under the condition of hypoxia.

Conclusion

Our investigation shows that Radix Astragali increased the PWC_{170}, VO_2max and step index in humans. The anti-fatigue activity of Radix Astragali is associated with an accelerated elimination of BLA, BUN and MDA, and with an increased of SOD, suggesting that Radix Astragali could delay the onset of fatigue in plateau environment, and accelerate the elimination of fatigue, which will provide an experimental foundation for the development of an anti-fatigue traditional Chinese drug application of Radix Astragali for use in the plateau.

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Disclosure of conflict of interest

None.

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