Effects of salidroside on exhaustive exercise-induced oxidative stress in rats

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Abstract. Intense exercise increases oxygen consumption and may produce an imbalance between reactive oxygen species (ROS) and antioxidants, inducing oxidative stress as a result of increased ROS production. Exogenous antioxidants may prevent oxidative damages since they are able to detoxify certain peroxides by scavenging the ROS produced during exercise. The aim of this study was to evaluate the effects of salidroside on exhaustive exercise-induced oxidative stress in rats. A total of 40 animals were randomly divided into four groups of ten rats each: control (C), low-dose salidroside-treated (LT), middle-dose salidroside-treated (MT) and high-dose salidroside-treated (HT) groups. The rats in the treated groups received salidroside (25, 50 and 100 mg/kg, respectively) intragastrically (ig) and the rats in the control group received drinking water ig for 4 weeks. After 4 weeks, the rats performed an exhaustive swimming exercise and exhaustive swimming times were recorded. The malondialdehyde (MDA), catalase (CAT), superoxide dismutase (SOD), glutathione peroxidase (GSH-Px) and glycogen levels in the liver tissues of the rats were measured. The data revealed that salidroside was able to elevate the exercise tolerance and increase the liver glycogen levels of the rats following exhaustive exercise. Salidroside was also able to reduce MDA levels and enhance the activities of antioxidant enzymes (CAT, SOD and GSH-Px) in the liver tissues of the rats. The results from this study indicate that salidroside is effective in the prevention of oxidative stress following exhaustive exercise.

Introduction

Cells continuously produce free radicals and reactive oxygen species (ROS) as part of their metabolic processes. These free radicals are neutralized by an elaborate antioxidant defense system consisting of enzymes, including catalase (CAT), superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px), and numerous non-enzymatic antioxidants, including vitamin E, vitamin A, vitamin C, glutathione and uric acid (1,2). Intense exercise increases oxygen consumption and may produce an imbalance between ROS and antioxidant levels, inducing oxidative stress as a result of increased ROS production (3). Indeed, exercise-induced oxidative stress leads to the destruction of tissue and cell macromolecules, including lipids, proteins and nucleic acids (4-6). It has also been suggested that exercise-induced oxidative stress may be associated with muscle fatigue, muscle damage and a decrease in physical performance (7-9). Antioxidants are substances that help to reduce the severity of oxidative stress, either by forming a less active radical or by quenching the reaction. It has been demonstrated that exogenous antioxidants may prevent oxidative damage since they are able to detoxify certain peroxides by scavenging the ROS produced during exhaustive exercise (10).

Rhodiola rosea ("golden root" or "Arctic root") is widely distributed at high altitudes in the Arctic and in mountainous regions throughout Europe and Asia (11). It has been widely used as a hemostatic, antitussive, tonic and endermic liniment for the treatment of burns and contusions in traditional Chinese medicine (12). Salidroside, 2-(4-hydroxyphenyl)ethyl β-D-glucopyranoside, the main active compound of Rhodiola rosea, is reported to exert antiviral, antiabetic, antifatigue, antiaging, neuroprotective and hepatoprotective effects (13-16). In addition, several studies have indicated that salidroside is an effective antioxidant and free radical scavenger (17-19). However, the effects of salidroside on the oxidative stress induced by exhaustive exercise have not yet been elucidated. In this study, exhaustive exercise was selected as the method of inducing oxidative stress in rats and the effects of salidroside on the exhaustive exercise-induced oxidative stress in the rat liver tissue were investigated.

Materials and methods

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Bioengineering Institute (Nanjing, China). All other chemicals and reagents were of analytical grade and were obtained from the usual commercial sources. Deionized water was used to prepare all solutions and in all experiments.

**Animals and grouping.** Male Sprague-Dawley (SD) rats (220-250 g) were purchased from the Animal Experiment Center of Tianjin University (Tianjin, China). The animals were housed at a temperature of 18-20°C and a humidity of 65-69% and were submitted to a 12-h light/dark cycle. The rats had unrestricted access to tap water and standard rat chow. All procedures involving the use of laboratory animals were carried out in accordance with the National Institutes of Health guidelines. Following an adaptation period of a week, 40 animals were randomly divided into four groups of ten rats each: control (C), low-dose salidroside-treated (LT), middle-dose salidroside-treated (MT) and high-dose salidroside-treated (HT) groups. The rats in the treated groups received salidroside (25, 50 and 100 mg/kg, respectively) intragastrically (ig) and the rats in the control group received drinking water ig for 4 weeks.

**Exhaustive swimming exercise.** After 4 weeks, the rats performed an exhaustive swimming exercise in an acrylic plastic pool (90x45x45 cm) filled with water maintained at a temperature of 36±2°C. The water depth, 35 cm, was set so that the rats could not rest by supporting their tails on the bottom of the pool. Each rat had a weight attached (5% body weight) to its tail for the duration of the swim-to-exhaustion exercise. The animals were assessed as being exhausted when they failed to rise to the surface of the water to breathe within 7 sec (20,21). The exhaustive swimming time was recorded in min for each rat.

**Biochemical parameters analysis.** At the end of exhaustive swimming exercise, all rats were immediately anesthetized with ethyl ether. Liver tissue was extracted and frozen in liquid nitrogen for storage at -80°C until required for MDA, CAT, SOD, GSH-Px and glycogen analysis. All biochemical parameters were tested following the recommended procedures provided in the assay kits.

**Statistical analysis.** The data are expressed as the mean ± SD based on the indicated number in the experiment. All analyses of data were carried out using the Statistical Package for Social Sciences (version 11.0; SPSS, Inc., Chicago, IL, USA). The results were analyzed using one-way analysis of variance followed by a Student's t-test for comparison between various treatment groups. *P*<0.05 was considered to indicate a statistically significant result.

**Results and Discussion**

**Effect of salidroside on the exhaustive swimming time of rats.** Swimming was selected as a model for exercise performance, since swimming appears to be natural behavior for rodents and humans (22,23). As shown in Fig. 1, the exhaustive swimming times of the rats in the LT, MT and HT groups were significantly prolonged compared with those in the control group (*P*<0.05), and were 1.52, 1.80 and 1.96 times longer than in the control group, respectively. These results suggest that salidroside is able to elevate the exercise tolerance of rats.

**Effect of salidroside on the liver glycogen levels of rats.** The contribution of glycogen to energy production during exhaustive exercise is necessary since glycogen may be degraded rapidly to produce ATP aerobically and anaerobically (24,25). The energy for exercise is derived initially from the breakdown of glycogen and later from circulating glycogen released by the liver and from non-esterified fatty acids. Therefore, increased liver glycogen storage levels are conducive to enhancements of endurance and locomotory capacity (26). As shown in Fig. 2, the liver glycogen levels of the rats in the LT, MT and HT groups were significantly increased compared with those in the control group (*P*<0.05). These results suggest that salidroside is able to significantly increase the liver glycogen levels of the rats following exhaustive exercise by improving the glycogen reserve, reducing the glycogen consumption during exercise or both.

**Effect of salidroside on the MDA levels in the liver tissues of rats.** Oxidative stress induced by exhaustion exercise may produce ROS. The production of ROS is harmful to the mitochondria in the cell as the ROS affect the functioning
of the mitochondria, causing them to lose their efficacy as components of the electron transport chain, which may also lead to aging or fatigue. This type of oxidation injury to the mitochondria results in lipid peroxidation and causes cell damage (27). MDA, a metabolite of phospholipid peroxidation, is a popular marker of living body oxidative damage (28). As shown in Fig. 3, the MDA levels in the liver tissues of the rats in the LT, MT and HT groups were significantly decreased compared with those in the C group (P<0.05). These results suggest that salidroside reduces lipid peroxidation.

Effect of salidroside on the CAT, SOD and GSH-Px levels in the liver tissues of rats. CAT, SOD and GSH-Px are regarded as the first line of defense of the antioxidant enzyme system against ROS generated during exhaustive exercise (29). SOD dismutates superoxide radicals to form H₂O₂ and O₂. GPH-Px is an enzyme responsible for reducing H₂O₂ or organic hydroperoxides to water and alcohol, respectively. CAT catalyzes the breakdown of H₂O₂ to form water and O₂ (30,31). As shown in Table I, the CAT, SOD and GSH-Px levels in the liver tissues of the rats in the LT, MT and HT groups were significantly increased compared with those in the C group (P<0.05). These results suggest that salidroside promotes increases in the activities of antioxidant enzymes (CAT, SOD and GSH-Px), which indicates that salidroside has beneficial effects on the attenuation of the oxidative stress induced by exhaustive exercise.

In conclusion, this study demonstrates that salidroside is able to elevate the exercise tolerance and increase the liver glycogen levels of rats following exhaustive exercise. Salidroside is also able to reduce MDA levels and enhance the activities of antioxidant enzymes (CAT, SOD and GSH-Px) in the liver tissues of rats. These findings indicate that salidroside is effective in preventing oxidative stress following exhaustive exercise. Therefore, salidroside may be used as an antioxidant supplement for competing athletes who participate in exhaustive endurance events.

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References