Effect of *Eleutherococcus senticosus* and Its Components on Rectal Temperature, Body and Grip Tones, Motor Coordination, and Exploratory and Spontaneous Movements in Acute Stressed Mice

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A water extract from *Eleutherococcus senticosus*, syringin and syringaresinol di-O-glucoside were tested for their effect on physical conditions in mice subjected to acute oscillation. The water extract served to prevent the stress-induced decrease in rectal temperature and body and grip tones, and to accelerate recovery from decreases in body and grip tones. Syringin functioned to prevent the stress-induced decreases in grip tone and exploratory movement, and to accelerate recovery from the decreases in grip tone, exploratory movement and spontaneous movement, and syringaresinol di-O-glucoside to prevent the stress-induced decreases in exploratory and spontaneous movements and to accelerate recovery from such conditions.

**Keywords**—*Eleutherococcus senticosus*; syringin; syringaresinol di-O-glucoside and stress

Root of *Eleutherococcus senticosus* (Rupr. & Maxim.) Harms has been used for about thirty years in the Far Eastern part of USSR as a general restorative, tonic and adaptogen which enhances general non-specific host resistivity to various stresses. Berkman and Dardymov\(^1\) reported that *E. senticosus* possessed an adaptogenic activity, and was capable of enhancing host resistance to various adverse influence of physical, chemical and biological nature. They also reported that the spectra of pharmacological action of *E. senticosus* and that of ginseng (*Panax ginseng* C.A. Mayer) were essentially the same. However *Eleutherococcus senticosus* and ginseng are not used in exactly the same way in Chinese medicine. *Eleutherococcus senticosus* is listed as Ciwuji, one of Wuji in ancient Chinese herbal literature. In China, there are 26 species of Acanthopanax plants growing all over the country, and those Acanthopanax plants have been used as Wuji in Chinese materia medica, for over hundreds of years.\(^2\) Wuji has long been esteemed as a corroborant drug used for curing bronchitis and as Bu-Yang-Yaw, a tonic in Chinese medicine which has been believed to invigorate physical energy, to nourish the vigour, to strengthen the skeleton and tendon, to build up one’s ambition, and to be good for anti- old and prolonging life after long administration.\(^3\)

In our previous report,\(^3\) a simple assay method was established for the evaluation of fatigue-preventing and recovery accelerating effect of drugs, and ginseng and its components were assayed for such activities. In the present research *Eleutherococcus senticosus* and its components, *i.e.* syringin and syringaresinol di-O-glucoside, were tested for their effect on prevention of fatigue and on recovery from exhausted states by that method.

**Materials and Methods**

A cold water extract (82.0 g) from *Eleutherococcus senticosus* (Rupr. & Maxim.) Harms (1.0 kg) from Heilongjiang Province (Botanicals Internationals, Inc.) and syringin and syringaresinol di-O-glucoside prepared according
Eleutherococcus senticosus Root (1.0 kg) 
extracted with MeOH (1.0 l) 
MeOH ext. 
partitioned between BuOH and H₂O 
BuOH layer (22.0 g) 
H₂O layer 
Fr-1 (9.8 g) Fr-2 (11.0 g) Fr-3 (1.7 g) H₂O eluate (3.3 g) MeOH eluate (14.2 g) 
EtOAc layer (4.1 g) H₂O layer (5.9 g) insoluble portion (0.86 g) 
partitioned between EtOAc and H₂O 
H₂O eluate (1.2 g) MeOH eluate (4.7 g) 
partitioned between EtOAc and H₂O 
H₂O layer 
H₂O eluate (1.0 g) MeOH eluate (0.15 g) 

I : syringaresinol di-O-glucoside 
II : syringin

Fig. 1.

to the procedure described in Fig. 1 were used. The drugs were given orally to mice 10 min before or immediately after the enforced exercise. Four weeks old male mice of ddY-strain, obtained from Shizuoka Farm Inc. were divided into groups of 10 animals and kept in a stainless steel cage (14 × 30 × 20 cm) placed in a room of constant temperature of 22 ± 2°C. After a week, ten mice were put in a steel box, in which 12 g fresh wood cuttings had been spred, and were subjected to 4 hr oscillation movement as enforced exercise to produce a fatigue state. The oscillation used was of 129 excursions per min, with an amplitude of 12.3 cm. Then the fatigued state was evaluated by rectal temperature (RT), body and grip tones (sliding angle (SA) and spring balance (SB)), motor coordination (rotating rod (RR)) and exploratory and spontaneous movements (exploratory movement (EM) and motor activity (MA) tests). The RT test was performed with an ordinary thermometer in the usual manner. In SA test a mouse was placed on plastic plate and the plate was tilted gradually (103°C per min). The critical angle at which the mouse fell was taken as the sliding angle. In SB test, a mouse was placed on a small metal net which was connected to a spring balance. The mouse is pulled backwards by the tail. The reading of the balance when the mouse failed to cling to the net, was automatically recorded on a kymograph. Each mouse was subjected to such trials two or three times to give its average. In the RR test, a plastic rod with a diameter of 3.2 cm was rotated at a rate of 12 rpm. Only those mice which kept on staying on the rotating rod for more than 5 min in two successive trials, were used in the experiment. In the RR test, any mice fell down in 3 min were taken as having motor incoordination. The apparatus used in the EM and MA tests, consisted of a box with three compartments: Each of the two outer bright compartments were connected to the dark compartment in the center through a round opening with a shutter. In the EM test, a mouse was placed in the outer bright compartment and 1) the time the mouse needed to enter the middle compartment after the first shutter was opened, was recorded. When the mouse entered into the compartment, the first shutter was closed. And 2) the time mouse needed to climb up to the opposite second hole after the second shutter was opened, and 3) the time the mouse needed actually enter the third bright compartment, were recorded. In the graphs of EM test shown in Figs. 2-7, the lowest portion of each bar shows the time which the mouse placed in the first compartment needed to pass into the middle dark compartment, the middle portion of the bars the time the mouse needed to climb onto the second hole and the top portion the time the mouse needed to move into the second bright compartment. In the MA test, the number of times that a mouse climbed up the second hole, was counted during the 30 min test period. In graphs of MA test in Figs. 2-7, the bar shows percent ratios of the number of times that a mouse reached the second hole during the test period to that in the control trial performed on the day before the test at the same hour of the day. Details of the oscillation apparatus and the 5 tests performed were described by Takagi et al.4 In our experiment, drugs were given 10 min before the enforced oscillation exercise, and the 5 tests were performed immediately after and 30 min after the enforced exercise to evaluate the preventive effect and recovery accelerative effect of the drugs. In another experiment, drugs were given immediately after the enforced exercise, and the 5 tests were performed 30 min and 2 hr after the enforced exercise to assess their recovery accelerative effect.

Results and Discussion

Administration of a water extract from Eleutherococcus senticosus before oscillation exercise prevented

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Stars indicate significant difference from control (Student's t-test, **: p<0.01, *: p<0.05 and (*) : p<0.10).

Recovery Accelerative Effect from Exhausted States of Water Extract of Eleutherococcus senticosus on Rectal Temperature, Body and Grip Tones, Motor Coordination, and Exploratory and Spontaneous Movements in Acute Stressed Mice

The results are shown in Fig. 2. When it was given after the oscillation stress at a dose of 1,000 mg/kg, it accelerated recovery from the decreased body tone significantly 30 min after the administration. It was found to have no effect on the decreases in rectal temperature, grip tone, and exploratory and spontaneous movements, and motor incoordination, when tested 30 min and 2 hr after the administration. The results are shown in Fig. 3. Fatigue preventive effect of the water extract, especially on body and grip tone decrease, was apparently more pronounced than the recovery accelerative effect. When syringin was administered before the exercise, it prevented the decreases in grip
tone at a dose of 100 mg/kg and exploratory movement at a dose of 50 mg/kg significantly, but no recovery accelerative effect was observed 30 min after the oscillation exercise. Results are shown in Fig. 4. When it was given immediately after the oscillation, syringin accelerated recovery from decreased grip tone at doses higher than 25 mg/kg, 30 min after the oscillation, and from lowered exploratory and spontaneous movements 2 hr after oscillation at a dose of 100 mg/kg. Results are shown in Fig. 5. When syringaresinol di-O-glucoside was given before the oscillation at doses higher than 50 mg/kg, it prevented decreases in exploratory and spontaneous movements significantly and accelerated recovery from decreased exploratory movement significantly at a dose of 100 mg/kg. However it did not prevent decreases in body and grip tones, and rectal temperature as a water extract from Eleutherococcus senti-
Fig. 6. Preventive Effect for Fatigue of Syringaresinol di-O-glucoside on Rectal Temperature, Body and Grip Tones, Motor Coordination, and Exploratory and Spontaneous Movements in Acute Stressed Mice

Results are shown in Fig. 6. When it was given immediately after the oscillation, syringaresinol di-O-glucoside also accelerated recoveries from decreased exploratory and spontaneous movements significantly at doses of 25 and 100 mg/kg, 30 min after oscillation. It does not accelerated recovery from fatigued states, and has no effect on decreased rectal temperature, body and grip tones and motor in coordination. Results are shown in Fig. 7. Effect of syringin or of syringaresinol di-O-glucoside was not exactly the same as that of a water extract from *Eleutherococcus senticosus*. The water extract had effect on body and grip tones, and its fatigue preventive effect was more pronounced than its recovery accelerative effect. Syringin was shown to have fatigue preventive effect and recovery accelerative effect of the same extent. Syringaresinol di-O-glucoside was shown to have effect on exploratory and spon-
taneous movements. And its recovery accelerative effect was stronger than its preventive effect. The water extract showed stronger effect on body and grip tones than syringin, and syringaresinol di-O-glucoside showed stronger effect on exploratory and spontaneous movements than syringin. Such difference among the pharmacological effects of water extract, syringin and syringaresinol di-O-glucoside suggested that syringin and syringaresinol di-O-glucoside are not the only pharmacologically active components in the crude drug, though these two compounds definitely play an important and significant role in the fatigue preventive effect and recovery accelerative effect of *Eleutherococcus senticosus*. A number of pharmacologically active substances contained in *Eleutherococcus senticosus*, such as coumarine glycoside, glucose and fructose, may also contribute to the pharmacological effect of *E. senticosus* on acute oscillated mice.

References and Notes