Panax Ginseng Inhibits Maximal Electroshock Induced Convulsions in Mice

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Abstract. Epilepsy is a serious common neurological disease. Panax ginseng root has been identified as a potential therapy for many disorders. The present study investigated the possible anticonvulsant activity of Panax ginseng on maximal electroshock (MES) induced seizure in mice. Mice were divided into the following groups: Group A (control group): injected with normal saline then exposed to electric shock. Group B (test group): injected with sodium valproate (300 mg/kg, 600 mg/kg, 900 mg/kg). Then exposed to electric shock. Group C (test group): injected with Panax Ginseng (150, 250, 350 mg/kg) then exposed to electric shock. All animals were examined for motor coordination on rotarod test. We concluded that P. ginseng at moderate and high doses significantly decreased the HLE duration of convulsion in mice, denoting that P. ginseng has anticonvulsant effects. the antiepileptic activity of P. ginseng might be due to its antioxidative actions, anti-inflammatory, its regulating effect on sodium ion channels and/or due to its possible modulation of GABA receptor channel activity for further investigations.

Keywords: Panax ginseng, rotarod, anticonvulsant, motor coordination, electric shock, Epilepsy.

1. Introduction

Epilepsy is a serious common neurological disease. It usually leads to decreased quality of life with increased mortality and morbidity [1]. About 30% of patients with epilepsy do not respond well to the available antiepileptic drugs [2]. The use of classical and new antiepileptic agents is usually associated with increased incidence of adverse effects. Thus an important hope for many trails is to develop new anti-seizure agents with a good rate of success and less risk of side effects [3].

Panax ginseng root (Korean ginseng) is considered as one of the most valuable and widely used medicinal herb in Asian countries [4, 5]. It has been identified as a potential therapy for many disorders including anti-stress, anxiolytic, Alzheimer’s disease, cognitive impairment and dementia [6].

The goal of the present study is to screen the anticonvulsant activity of different doses of panax ginseng on maximal electroshock (MES) induced seizure in mice.

2. Material and Methods

2.1. Experimental animals. Adult male albino mice (weighting) (22-26 gm) were delivered from National Research Laboratory, College of Pharmacy Qassim University, Saudi Arabia, and kept in colony cages under standardized housing conditions and free access to tap water and food (Natural light-dark cycle, a temperature of 22±1°C). After 5 days of adaptation to laboratory conditions, the animals were divided randomly to the experimental groups. All tests were performed between 8.00 and 15.00 h and each mouse...
was used once. The experimental protocol was approved by the Ethics Committee of College of Pharmacy, Qassim University, Saudia Arabia.

2.2. Drugs and chemicals. 1. Panax ginseng (Ginsana capsule 100 mg).

2. Sodium valproate (Depakine 200 mg tablets), Sanofi Aventis

2.3. Maximal electroshock (MES) induced seizures test. A 50 HZ stimulus of 200 milliseconds duration was applied through saline wet ear electrode to improve electrode contact. Current intensity was increased in a step-wise manner from 1 to 30 MA to reach the current which causes convulsions without the death of the animals. 13 MA produced convulsions with tonic hind limb extension. This current was used throughout this study. The duration of seizure (i.e. hind limb tonic extension) following electroshock application to the mice was recorded.

2.4. Study design. Group A (control group): 18 mice were injected with normal saline then exposed to electric shock. Group B (test group): 18 mice were injected with sodium valproate (300 mg/kg, 600 mg/kg, 900 mg/kg). Then exposed to electric shock. Group C (test group): 18 mice were injected with Panax Ginseng (150, 250, 350 mg/kg), then exposed to electric shock. Each group was divided into three equal groups 6/each.

2.5. Rodent shocker. The apparatus used in Rodent Shoker TYP 21 (Harved apparatus GmbH Germany).

2.5.1. Assessment of motor coordination in mice. The effects of drug administration on the motor coordination of mice can be detected by ROTARODS LE 8200 (Panlab, S.L Spain).

A central drum divided into sections for individual animals rotate from 4 to 40 revolutions per minute in 0.5 to 10 minutes, either at a constant speed or at a steady acceleration rat. The time, the animal spends from the beginning of the test until the animal falls from the drum in each section (TS) is taken as a measure of coordination [7].

2.5.2. Procedure. The acceleration time used in this study is 10 min. Before starting a test, the animals have to be trained for 3-4 days to be able to walk on Rotarod. To start a test, position the animals on their partitions on Rotarod, then adjust the run-stop button to the middle position and left the needed leavers, after that use the run-acceleration button to adjust the acceleration time then press a start-stop button. At this time, the speed and time counters will start to work. Once the animal fall, its counters will stop running [7].

2.6. Statistical analysis. The obtained variables were tabulated as mean± SD. Comparison between different groups was made using one way analysis of variance (one-way ANOVA) followed by post Hock (least significant difference) LSD tests as described by Armitage and Berry [8]. The difference was considered to be significant when P<0.05 statistical package of social science (SPSS) (version 16).

3. Results

The results of the present study showed that, in the MES induced seizure model, sodium valproate at low, medium and high doses (300, 600, 900 mg/kg) showed significant anticonvulsive effects which represented by significant reduction of the duration of hind limb extension in the animals compared with the control untreated group (table 1,2). Furthermore, panax ginseng at low dose administration (500 mg/kg) showed no anticonvulsant effect. However, in moderate and high doses (250 mg/kg & 350 mg/kg) respectively panax ginseng showed a significant reduction in the duration of hind limb extension in mice compared with the control untreated group (Table 1,2).

In the present study, P. ginseng showed significant improvement in motor coordination estimated using Rotarod as evident by the insignificant change in the rotarod performance test between the P. ginseng treated and the control values. Moreover, on general observation no eyelid ptosis, bristling fur, weeping eyes were observed in the P. ginseng treated group. (Table 2)

4. Discussion

In this study Panax ginseng (P. ginseng) different doses were evaluated against MES induced convulsion in mice. MES induced seizure test is a widely used test to determine the potential antiseizure effects of different substances in rodents [9]. In the present work, P. ginseng at moderate and high doses significantly decreased the HLE duration of convulsion in mice, denoting that P. ginseng has anticonvulsant effects. These results are inconsistent with Choi et al., [10] who demonstrated that, the Korean red ginseng exerts anticonvulsant action in mice against picrotoxin and bicuculline induced seizure via the change in the brain GABA and glutamate contents.
Table 1: Comparison between the effects of Panax ginseng and Sodium valproate on the duration of hind limb extension in mice.

| Time (min) | Control group | Sodium valproate treated group | P. ginseng treated group |
|------------|---------------|--------------------------------|--------------------------|
|            | Low dose (300 mg/kg) | Moderate dose (600 mg/kg) | High dose (900 mg/kg) | Low dose (150 mg/kg) | Moderate dose (250 mg/kg) | High dose (350 mg/kg) per second |
| After 30   | 24.6 ± 0.51 A | 13.9 ± 0.5 B | 8.8 ± 0.7 C | 7.1 ± 0.1 C | 22.9 ± 0.5 A | 21.3 ± 0.4 D | 14.2 ± 0.8 B |
| After 60   | 24.6 ± 0.51 A | 12.8 ± 0.2 B | 8.3 ± 0.5 C | 6.9 ± 0.3 C | 22.5 ± 0.6 A | 21.1 ± 0.8 D | 13.9 ± 0.2 B |
| After 90   | 24.6 ± 0.51 A | 12.2 ± 0.8 B | 8.0 ± 0.5 C | 6.8 ± 0.8 C | 22.2 ± 0.9 A | 20.7 ± 0.8 D | 13.8 ± 0.2 B |
| After 120  | 24.6 ± 0.51 A | 11.8 ± 0.2 B | 7.8 ± 0.4 C | 6.8 ± 0.3 C | 22.2 ± 0.1 A | 20.3 ± 0.4 D | 13.6 ± 0.4 B |
| After 150  | 24.6 ± 0.51 A | 11.5 ± 0.4 B | 7.7 ± 0.4 C | 6.3 ± 0.6 C | 22.1 ± 0.1 A | 20.1 ± 0.7 D | 13.3 ± 0.8 B |
| After 180  | 24.6 ± 0.51 A | 11.1 ± 0.5 B | 7.6 ± 0.1 C | 5.8 ± 0.1 C | 22.1 ± 0.2 A | 20.1 ± 0.0 D | 13.0 ± 0.9 B |

* Values are expressed as mean ± SD.
* Values with common superscript capital letters are insignificantly different.

Table 2: Comparison between the effect of Panax ginseng and sodium valproate on muscle coordination in mice.

| Time (min) | Control group seconds | Group with sodium valproate (300 mg/kg) seconds | Group with P. ginseng (350 mg/kg) seconds |
|------------|------------------------|-----------------------------------------------|------------------------------------------|
| After 30   | 7.00 ± 0.24 A          | 3.17 ± 0.17 B                                | 7.10 ± 0.20 C                            |
| After 60   | 6.96 ± 0.30 A          | 2.79 ± 0.17 B                                | 7.00 ± 0.19 C                            |
| After 90   | 7.10 ± 0.23 A          | 3.85 ± 0.27 B                                | 7.11 ± 0.20 C                            |
| After 120  | 7.05 ± 0.22 A          | 2.80 ± 0.14 B                                | 6.95 ± 0.23 C                            |
| After 150  | 7.15 ± 0.26 A          | 3.17 ± 0.17 B                                | 7.00 ± 0.18 C                            |
| After 180  | 6.95 ± 0.25 A          | 3.87 ± 0.27 B                                | 7.15 ± 0.25 C                            |

* Values are expressed as mean ± SD.
* Values with common superscript capital letters are insignificantly different.

Gupta et al., [11] also demonstrated that P. ginseng induced antiepileptic effect against PTZ induced kindling in rats.

There are many types of ginseng available for medical use. The most popular are Panax quinquefolius (American ginseng), Korean red ginseng and Panax ginseng (oriental ginseng). The active constituents vary according to the species [12].

The most active constituents of P. ginseng are ginsenoside Rb1, ginsenoside-Re, ginsenoside-Rd, and ginsenoside-Rg1 [13]. Seizures can be evoked by oxidative stress and free radicals accumulation under pathological conditions [14].

Kabuto et al., [15] demonstrated that antioxidant administration showed protective efficacy against iron-induced epileptic discharges in rats.

Lim et al. [16] and Cantuti-Castelvetri et al. [17] showed that ginsenosides, the active components of P. ginseng, exerted potent antioxidant properties.

Zhou et al., [18] also demonstrated that ginsenoside-Re can improve mitochondrial function and reduce mitochondrial swelling via reduction of MDA brain content and up-regulation of the activity of superoxide dismutase.

Citraro et al. [19] demonstrated that, cyclooxygenase (Cox) which involved in the production of many Pro-inflammatory prostaglandins can play an important role in inflammation-induced seizure. Cox-2 in the brain reported to increase during and after seizures thus Cox-2 inhibitors able to reduce or even prevent the development of absence seizure in WAG/Rij rat [19].

de Oliveira et al., [20] also showed that ginsenoside-Ro has an anti-inflammation action against muscle damaging.

Indeed P. ginseng targeted multiple points within the inflammatory cascade as it can inhibit inducible nitric oxide synthase (iNOS), cyclooxygenase-2 (Cox-2) and nuclear factor kappa B [21]. Wang et al., [22] also demonstrated that, ginsenoside-Rb1 decreases expression of Cox-2 mRNA in brain tissue, reduces inflammation and nerve damage. They also showed that ginsenoside-Rg1 can improve memory
and learning functions in rats, regulate cell survival and neurogenesis, and inhibit the activity of caspase 3.

Wang et al., [22] also showed that ginsenoside Rd can reduce oxidative and inflammatory damage, protect mitochondria and reduce cell apoptosis in a wide range of tissues.

Liu et al., [12] showed that the ginsenoside Rh1 in P. ginseng has been shown to produce a neuroprotective action by blocking the sodium channels and it also has been shown to regulate GABAergic transmission Indeed MES induced seizures are sensitive to sodium channels blocking agents.

It can be concluded, from all of the previous works and our study that, the antiepileptic activity of P. ginseng might be due to its antioxidative actions, anti-inflammatory, its regulating effect on sodium ion channels and/or due its possible modulation of GABA receptor channel activity for further investigations.

Competing Interests

The authors declare no competing interests.

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