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SHORT COMMUNICATION

ANTIEPILEPTIC ACTIVITY OF PANAX GINSENG AGAINST PENTYLENETETRAZOLE INDUCED KINDLING IN RATS

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Abstract : In the present study, Panax ginseng was evaluated for its antiepileptic activity against pentylenetetrazole (PTZ) induced chemical kindling in rats. PTZ was injected at the dose of 30 mg/kg, i.p. on alternate days and the occurrence of generalized tonic clonic convulsions were considered as the end point. One group received Panax ginseng every day, at a dose of 100 mg/kg, 30 min prior to PTZ injection whereas the other group received an equal volume of distilled water to serve as control. In a separate group the rats were evaluated for motor performance tests after Panax ginseng. The rats treated with Panax ginseng showed significant protection as compared to vehicle treated PTZ injected rats. The study suggests to potential of Panax ginseng against seizures.

Key words : Panax ginseng seizures chemical kindling rats

INTRODUCTION

Panax ginseng C.A. Meyer, is a widely used traditional oriental plant. The root of this plant has been used for thousands of years for its rejuvenating and tonic effects on the body and mind. In traditional Chinese and Korean system of medicine, it is claimed to possess anti-stress, anti fatique, mood stabilizing and cognition facilitating properties (1).

Experimentally, Panax ginseng has also been reported to have beneficial effects in various neurological disorders such as neuropsychiatric symptoms associated with ageing, cerebral vascular insufficiency and Alzheimer's disease (2–5).

It was considered worthwhile to investigate the effect of Panax ginseng against pentylenetetrazole (PTZ) induced chemical kindling model, which represents generalized tonic-clonic

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convulsions to evaluate its antiepileptic potential.

METHODS

Animals

Male Wistar rats weighing 200–250 g were used. The animals were obtained from the central animal facility of All India Institute of Medical Sciences, New Delhi and stock bred in the departmental animal house. The rats were group housed in polyacrylic cages (38 × 23 × 10 cm) with not more than 4 animals per cage and maintained under standard laboratory conditions with natural dark and light cycle. They were allowed free access to standard dry rat diet and tap water ad libitum. All procedures described were reviewed and approved by the Institutional Committee for Ethical Use of Animals. Each group consisted of 7 animals. The rats were divided into 3 groups : (1) vehicle treated PTZ injected rats (2) Panax ginseng treated PTZ injected rats (3) Panax ginseng treated rats for motor performance tests.

Drugs

PTZ (Sigma, St Lo, MO, USA) was dissolved in distilled water. Concentrated (100%) pure red Korean Panax ginseng (Korean ginseng products Co Ltd) containing 60 mg/g of ginsenoside was used. PTZ was injected intraperitonially (30 mg/kg) using a 26-gauge needle on alternate days. Panax ginseng was administered orally using an intra gastric cannula every day at a dose of 100 mg/kg, whereas distilled water was administered as vehicle in the PTZ treated rats. The dose of P. ginseng was selected on the basis of previous reports, which have utilized dosage ranging from 20–1000 mg/kg (6, 7).

Chemical kindling in rats

Chemical kindling was induced by intraperitoneal injection of subconvulsant dose of PTZ, 30 mg/kg in rats on alternate days, 3 times a week (8). The rats were observed for a period of 30 min after PTZ and seizure activity was scored using a scoring system from 0–5 (Table 1). Animals showing stage 5 seizures, not necessarily consecutive, were considered to be kindled after which the PTZ treatment was stopped. To ascertain whether the increased sensitivity to PTZ was persistent, the rats were challenged with 30 mg/kg PTZ on 3rd and 10th day after the PTZ treatment had ended.

Stage	*Symptoms*
0	No change
1	Hyperactivity, restlessness, vibrissae twitching
2.	Head nodding, head clonus, myoclonic jerks
3.	Unilateral or bilateral limb clonus
4.	Forelimb clonic seizures
5	Generalized clonic seizures with loss of righting reflex

Motor coordination

Rota rod was used to evaluate the muscle coordination in the Panax ginseng

treated rats. The rats were first conditioned to the accelerating rota rod (Ugo Basil). Each animal received a training session on the rota rod set at a constant speed of 8 rpm and was tested until they achieved the criterion of remaining on the rotating spindle for 60 s. Each rat then received a single trial on the accelerating rota rod in which the spindle increased in speed from 4–40 rpm over a period of 5 min, which acted as baseline value. The next day, the rats were pretreated with Panax ginseng and allowed to move on the accelerating rota rod using the same protocol (9).

Statistical analysis

The results are expressed as Mean ± S.E.M. Statistical analysis was performed by the means of Students t test. $P<0.05$ represents the level of significance.

RESULTS

Induction of PTZ kindling in normal rats

Chemical kindling in rats was established by administration of sub convulsant doses of PTZ (30 mg/kg, i.p.), 3 times a week on every alternate day. Development of fully kindled stage 5 seizures, i.e. generalized tonic clonic seizure in these animals was observed after 14 injections of PTZ. This kindling was confirmed when the rats were rechallenged on the 3rd and the 10th day after PTZ treatment ended.

Effect of Panax ginseng on PTZ kindling in rats

Of the group which received Panax ginseng (100 mg/kg, p.o.) daily, none of the rats developed kindling. The mean score observed in the Panax ginseng treated rats was 1 as compared to 5 in the vehicle treated PTZ rats.

Effect of Panax ginseng on motor coordination

To evaluate whether the dose used of Panax ginseng, had any effect on motor coordination, the rats were pretreated with Panax ginseng (100 mg/kg), 30 minutes after which the rats were placed on the accelerating rota rod. It was observed that there was insignificant difference ($P>0.05$) in the time spent on the rotating spindle between the Panax ginseng as compared to the baseline (control) values. The mean score being 149 ± 10.1 and 127 ± 8 s respectively.

DISCUSSION

In the present study, it was observed that administration of subconvulsant dose of PTZ on alternate days resulted in stage 5 seizures after 14 injections. PTZ kindling is an acknowledged animal model for epilepsy and refers to a phenomenon in which repeated injection of a convulsant causes gradual seizure development culminating in generalized tonic clonic seizures and is an appropriate model resembling epilepsy in humans (10). In the PTZ rats treated with Panax ginseng (100 mg/kg, p.o), a significant protection was observed. Panax ginseng treated rats showed behavioral changes only up to stage 1 on the seizure score as compared to stage 5 in the vehicle treated PTZ rats. Recently, Mattei et al showed that

Panax ginseng causes reduction in motor activity, eyelid ptosis and bristling fur (11). Therefore, in the present study, the effect of Panax ginseng on motor activity was evaluated using rota rod. It was observed that dose of 100 mg/kg, p.o, used in the study, did not cause any motor impairment as evident by the insignificant change in the rota rod performance test between the Panax ginseng treated and the control values. Moreover, on general observation no eyelid ptosis, bristling fur, weeping eyes were observed in the Panax ginseng treated group.

Free radicals have been implicated in the development of seizures under pathological conditions (12, 13) and the protective efficacy of antioxidant treatments against some types of seizures has been reported (14–16). In our laboratory, we have shown the beneficial effect of trans resveratrol, an antioxidant, against kainic acid induced seizures and its subsequent increased oxidative stress in rats suggesting the potential of antioxidants in epilepsy (17).

Also, recent findings suggest that free radicals are produced during PTZ induced kindling model in rats and may contribute in the biochemical sequelae of events leading to seizure induced cell death (18, 19). Ginsenosides are the active components of Panax ginseng and believed to be responsible for its medicinal properties (6). They have shown potent antioxidant properties in various experimental studies (2, 3, 11). The antiepileptic effect observed of Panax ginseng against PTZ induced kindling model of epilepsy may be attributed to its antioxidant property though other mechanisms cannot be ruled out.

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