Anticonvulsant Effects of Aqueous Extract of *Glycyrrhiza glabra* Root in PTZ-Induced Seizure in Mice

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**Abstract:** In this study, anticonvulsant effects of aqueous extract of *G. glabra* were investigated in mice. *G. glabra* extract, diazepam and normal saline were injected intraperitoneally at 50-300 mg kg⁻¹, 0.5-1 mg kg⁻¹ and 10 mL kg⁻¹, respectively, 30 min before pentylentetrazole (90 mg kg⁻¹, i.p.). Aqueous extract at a dose of 300 mg kg⁻¹ delayed the onset time of the seizure and decreased the duration of seizure significantly compared to the control. The duration of seizure was also significantly decreased at doses 60-200 mg kg⁻¹. In conclusion, the aqueous extract of *glycyrrhiza* root possesses anticonvulsant activities which may be effective in the management of petit mal seizure.

**Key words:** *Glycyrrhiza glabra*, pentylentetrazole, seizure, anticonvulsant, aqueous extract, herbal medicine

**INTRODUCTION**

Licorice, scientifically named *Glycyrrhiza glabra*, belongs to the Leguminosae family. It is a perennial herb native to the Mediterranean region, Middle East and now widely cultivated throughout Europe (Ody, 2000). The most important bioactive components of licorice root are glycyrrhizin and glycyrrhetinic acid (GLA) (Blumenthal et al., 2000). Most of the noted activities shown by glycyrrhiza extract are attributed to its aglycone saponins, 18 β-glycyrrhetinic acid (GLA). GLA has a semi steroidal structure and its synthetic derivative, carbonoxolone has been used for gastroduodenal peptic ulcer treatment (Turpie and Thomson, 1965). Previous studies have also shown anticonvulsant effects in mice (Hosseinzadeh and Nassiri-Asl, 2003; Gareeri et al., 2004).

Also, licorice extract has shown memory improvement activity in mice (Dhingra et al., 2004) and glabridin as a licorice constituent has antidepressant effects by the inhibition of serotonin reuptake (Ofir et al., 2003; Dhingra and Sharma, 2006). In this study we examined anticonvulsant effects of *Glycyrrhiza glabra* extract using pentylentetrazole (PTZ) induced seizure as a petit mal epilepsy model in mice.

**MATERIALS AND METHODS**

**Animals:** Sixty male BALB/c mice, 25-30 g were obtained from the animal house of Razi Institute (Karaj, Iran). They were housed in colony rooms with 12/12 h light/dark cycle at 21±2°C and had free access to food and water. All animal experiments were carried out in accordance with Qazvin University of Medical Sciences, Ethical Committee Acts.

**Preparation of extracts:** *Glycyrrhiza glabra* was collected from vikin (a village in Qazvin province, Iran) in 2006 and authenticated by Qazvin Agriculture and National Resources Research Center, Iran (Voucher No. 532). Dried roots were ground and the powder was extracted using aqueous decoction. In the decoction method, 100 g of the powder were added to 1 L of boiling water for 15 min and then filtered through a cloth. The extract was then concentrated under reduced pressure to the desired volume. The yield of the extract was 10% (w/w). The extract was diluted with saline.

**Chemicals:** Pentylentetrazole was obtained from Sigma. Diazepam was from Chemi Darou Pharmaceutical Co., Iran in the form of ampoule (2 mg/10 mL). All drugs were dissolved in normal saline solution.

**Anticonvulsant activity:** The mice were divided into nine groups with seven mice in each group. Six groups received intraperitoneal injections of *G. glabra* aqueous extract at increasing doses of 50, 60, 80, 100, 200 and 300 mg kg⁻¹, 30 min before the administration of pentylentetrazole (90 mg kg⁻¹, i.p.). Other groups of mice...
were injected with normal saline and diazepam (0.5-1 mg kg⁻¹, i.p.) before PTZ was given. After administration of PTZ, each animal was placed into an individual plastic cage for observation lasting 1 h. The time until the onset of clonic convulsions, the duration of clonic convulsions and the percentage of seizure and mortality protection were recorded (Vida, 1995). The general clonus was characterized by forelimb clonus followed by full clonus of the body.

**Statistical analysis:** The dose of *G. glabra* to produce an anticonvulsant (ED 50) effect in 50% of animals and its associated 95% confidence limits was calculated by Litchfield and Wilcoxon methods (PHARM/PCS Version 4). Data were expressed as mean values±SEM and tested with variance analysis ANOVA, followed by the multiple comparison tests to Tukey-Kramer for the anticonvulsant activity. Results with *p*<0.05 were concluded to be significant.

**RESULTS AND DISCUSSION**

In the PTZ model ED 50 value of *G. glabra* aqueous extract was: 273.66 mg kg⁻¹ (%95 CI: 133.98, 558.92 mg kg⁻¹). Licorice extract at the dose of 300 mg kg⁻¹ could significantly delay the onset of seizure and reduce the duration of seizure compared to control. At lower doses 60-200 mg kg⁻¹, the duration of seizure only reduced compared to the control (Table 1). The percentage of seizure protection increased dose dependently, but mortality protection did not change by dose enhancement.

The present study investigated the anticonvulsant effects of *G. glabra* using the PTZ model. Results indicate that aqueous extract of glycyrhrizic acid showed anticonvulsant effects in the PTZ model. Agents affecting the PTZ model can inhibit petit mal seizure (Vida, 1995). Thus, aqueous extract of glycyrhrizic acid may have action on this kind of seizure. Glycyrrhizic acid and its derivatives have been shown to inhibit gap junction channels (Davidson and Baumgarten, 1988). In the presence of bicuculline, glycyrrhizic acid abolished seizure-like activity *in vitro* guinea-pig brain preparation (De Curtis *et al.*, 1998). In earlier study, we reported that carbamazepine, the succinyl ester of glycyrrhizic acid, had anticonvulsant effects in the PTZ model and in this study glycyrrhizic extract was similarly shown to decrease the duration of seizure (Hossienzadeh and Nassiri-Asli, 2003). The inhibitory effects of 18β-glycyrrhetinic acid on gap junction channels of arteriolar smooth muscle, endothelial cells, renal pelvis, ureter and mesenteric small arteries were established (Yamamoto *et al.*, 1998; Santicioli and Maggi, 2000; Matchkov *et al.*, 2004).

| Table 1: Effects of *G. glabra* extract on PTZ-induced convulsion in mice |
|-----------------------------|---------------------|---------------------|
| Treatments (dose) | Onset (sec) | Duration (sec) |
| Normal saline (10 mL kg⁻¹) | 51.83±4.0 | 12.0±4.4 |
| Diazepam (0.5 mg kg⁻¹) | 48±3.9 | 3.5±0.4 |
| Diazepam (1 mg kg⁻¹) | 49±0.6 | 0.0±0.0 |
| G. extract (50 mg kg⁻¹) | 48±0.6 | 5.5±1.4 |
| G. extract (100 mg kg⁻¹) | 65±0.5 | 6.2±1.4 |
| G. extract (200 mg kg⁻¹) | 87±3.3 | 5.5±1.3 |
| G. extract (500 mg kg⁻¹) | 199±2.5 | 5.5±2.0 |
| G. extract (200 mg kg⁻¹) | 216±4.9 | 4.2±1.3 |
| G. extract (500 mg kg⁻¹) | 262±4.0 | 3.3±1.6 |

Normal saline, diazepam and G. extract were administered i.p., 30, 60 min, respectively before the injection of PTZ (90 mg kg⁻¹, i.p.). Values are the mean±SD for 7 mice; *p*<0.05, ***p*<0.001; Compared to saline group, Tukey-Kramer test

These studies suggest that a component of the anticonvulsant effects of the extract could be related to the inhibitory effects of glycyrrhetinic acid on gap junction channels. Also, there is some evidence that glycyrhetinic acid derivatives exert a variety of effects such as altering the activity of ion transport processes including ion channels and inhibition Na-'K'-ATPase (Terasawa *et al.*, 1992; Tare *et al.*, 2002). Glycyrrhiza extract displays multiple biochemical properties, all of which are possible contributors to its anticonvulsant effects. We concluded that aqueous extract of glycyrhriza root possesses anticonvulsant activity which may be effective in petit mal seizure. However, further studies are needed to describe the possible mechanism involved in the ameliorative effect of *Glycyrrhiza glabra* root in PTZ-induced seizure in mice.

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**REFERENCES**


