ANTI-CONVULSANT ACTIVITY OF AQUEOUS EXTRACT OF *PICRORRHIZA KURROA* LEAVES IN MICE

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Summary

Picrorrhiza kurroa is used traditionally in the treatment of epilepsy. In the present study, anti-epileptic efficacy of the aqueous extract of *Picrorrhiza kurroa* leaves on Maximal electroshocks (MES) and PTZ induced convulsions was investigated. In both the models, the aqueous extract of *Picrorrhiza kurroa* leaves at different dose levels (50mg/kg, 100mg/kg and 200mg/kg) significantly reduced the time spent in extensor phase. This indicates that *Picrorrhiza kurroa* possess anti-epileptic property similar to standard drug, Phenytoin. Results support the traditional use of the plant in the treatment of epilepsy. Thus *Picrorrhiza Kurroa* leaves could be regarded as favorable anti-convulsant drug.

Keywords: *Picrorrhiza kurroa*, Phenytoin , MES, PTZ

Introduction

Epilepsy is a neurological disorder that affects a wide range of people throughout the world. It is a disorder of brain characterized by unpredictable and periodic occurrence of a transient alteration of behavior due to the disordered, synchronous and rhythmic firing of populations of brain neurons. The current therapeutic treatment of epilepsy with modern antiepileptic drugs [AEDs] is associated with side-effects, dose related and chronic toxicity. Approximately 30% of the patients continue to have seizures with current AED therapy. Natural products from folk remedies have contributed significantly in the discovery of modern drugs and can be an alternative source for the discovery of AEDs with novel structures and better safety and efficacy profiles [1].

Picrorrhioza kurroa (Scrophulariaceae) also known as kutki, is a small perennial herb. It is a well known herb in the Aurvedic System of Medicines and is traditionally used for treatment of epilepsy [2,3]. Previously reported chemical constituents from *Picrorrhiza kurroa* include Kutkin, Kutkiol, Picroside I and Picroside II, Apocynin and androsin [4, 5, 6]. Current research on *Picrorrhiza kurroa* has focused on its hepatoprotective and immuno-modulating activity [7]. Since no detailed scientific data is available on the anti-convulsant activity of *Picrorrhiza kurroa* therefore the present study was undertaken.

Materials and Method

Drugs

Phenytoin (Epsoline) Zydus neuroscience, was used in this study.

Plant Material

The leaves of *Picrorrhiza kurroa* were collected from Chamba road, Kaddukhal, Mysoori (Uttranchal) and authenticated by Dr. Anjula Pandey, Taxonomist, National Herbarium of Cultivated Plants, National Bureau of Plant Genetic and Resources, New Delhi.

Experimental animals

Swiss albino mice weighing 18-25 g of either sex were used for the study. Institutional Animal Ethics Committee approved the experimental protocol**.** Animals were maintained under standard conditions in an animal house approved by Committee for the Purpose of Control and Supervision on Experiments on Animals (CPCSEA). (Approval No. 711/02/a/CPCSEA). They were fed with standard diet and water ad libitum.

Preparation of *Picrorrhiza Kurroa* leaves extract

The shade dried leaves of *Picrorrhiza kurroa* were coarsely powdered and extracted in cold water by stirring for 6 hrs and kept overnight at room temperature. After that supernatant was collected and evaporated to dryness at 100ºC under pressure in rotary evaporator. The *Picrorrhiza kurroa* leaves extract was triturated in 2% Gum Acacia suspension and administered at dose levels of 50mg/kg, 100mg/kg and 200mg/ kg p.o. [8].

Anti-Convulsant Activity

Maximal electroshock induced seizures

Maximal electroshock seizure model was used to evaluate the anticonvulsant activity of aqueous extract. Seizures were induced in mice by delivering electroshock of 50mA for 0.2 seconds by means of an electro- convulsiometer through a pair of ear clip

electrodes [9]. The test animals (n=6) received 50, 100, 200 mg/kg of aqueous extract orally and standard group received phenytoin (25 mg/kg) injected i.p. [10] and tested after 30 minutes for MES induced seizure response. All the experimental groups were compared with the control treated with vehicle.

PTZ-induced seizures

PTZ at the dose of 80 mg/kg (minimal dose needed to induce convulsions) was injected i.p. to induce clonic-tonic convulsions in mice. The test animals (n=6) received 50, 100, 200 mg/kg of aqueous extract orally and standard group received phenytoin (25 mg/kg) injected i.p. PTZ was injected i.p. 60 min after the administration of drug. Occurrence of HLTE and duration of seizures were noted. If no HLTE occurred during the time limit, the animals were considered protected [11].

Statistical Analysis [12]

All the results obtained from various activities, as described above, were analyzed statistically by using Student's t test and $p<0.05$ were considered significant. The results are summarized in the tables given below.

Results

The results of MES induced seizure model is shown in table 1 and that of PTZ model in table 2. In both the models, the aqueous extract significantly decreased the duration of extensor phase in a dose dependent manner.

Table 1: Effect of aqueous extract of *Picrorrhiza kurroa* leaves on Hind limb extension induced by MES in mice.

S.No.	Group	Dose (mg/kg)	Hind limb extension (Mean ± SEM)
1	Control		9.35± 0.4650
2	Phenytoin	25	1.06±0.3819[b]
3	PKAE	50	10.17±0.5706
4	PKAE	100	7.34±0.2608[a]
5	PKAE	200	5.67±0.1272[b]

Value are expressed as mean ± SEM (n =6)
[a]p<0.01, [b]p<0.001 as compared to control

Table 2: Effect of aqueous extract of *Picrorrhiza kurroa* leaves on PTZ induced seizures in mice.

S. No.	Group	Dose (mg/kg)	Onset Time (Sec)	Duration of HLTE (Sec)
1	Control	-	51.53±0.2108	37.25±0.5579
2	Phenytoin	25	0[b]	0[b]
3	PKAE	50	53.71±0.1536[b]	34.96±0.4121[a]
4	PKAE	100	55.83±0.2418[b]	32.78±0.6141[b]
5	PKAE	200	58.50±0.1807[b]	30.31±0.6269[b]

Values are expressed as mean ± SE (n=6)
[a]p<0.01, [b]p<0.001 as compared to control

Discussion

It was found from the above observations that PKAE has shown anticonvulsant activity against seizures induced by MES and PTZ in a dose dependent manner.

It was effective against MES induced seizures, since inhibition of the MES test predicts activity against generalized tonic-clonic and cortical focal seizures. PTZ is a most frequently used substance as well as an acute experimental model in the preliminary screening to test potential anticonvulsant drugs. Several biochemical hypotheses have been advanced involving the inhibitory GABAergic system and the system of the excitatory amino acid glutamate and aspartate [13]. The mechanism by which PTZ is believed to exert its action is by acting as an antagonist at the GABA receptor complex [14]. Drugs protecting against tonic-clonic seizures induced by PTZ are considered to be useful to control myoclonic and absence seizures in humans [15].

Therefore, the results obtained from the study suggest that aqueous extract of *Picrorrhiza kurroa* leaves has anti-convulsant property and the results verify its traditional use in epilepsy.

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References

1. Kaushik D., Khokra S. L., Kaushik P., Saneja A. and Arora D. Anticonvulsant Activity of *Mitragyna Parvifolia* Leaves Extract. Pharmacologyonline 2009; 3: 101-106.

2. Atal CK, Sharma ML, Kaul A et al Immunomodulating agent of plant origin. J. Ethanopharmacol 1986; 18:133-141.
3. http://www.satveda.com/kutki-powder.html
4. Dorch W, Stuper H, Wagner H et al. Anti-asthmatic effects of *Picrorrhiza kurroa*. Androsin prevent allergen and PAF-Induced bronchial obstruction in guinea pigs. Ins. Arch. Allergy appl. Immun 1995; 95:128-133.
5. Anadan R, Devaki T et al. Biochemical studies on the anti-hepatoxic, potential of *Picrorrhiza kurroa* on mitochondrial damage in D-galactosamine-induced liver intoxication in rats. Med. Sci. Res. 1998; 26:349-352.
6. Nandkarni's K.M, Nandkarni A.K. Indian Material Medica, Popular prakashan, Bombay, 1976; vol.1: 954.
7. Hyeung Sike Lee, Hyo Chan Ahn, Sae Kwang Ku, Hypolipemic effect of water extract of *Picrorrhiza rhizoma* in PX-407 induced hyperlipemic ICR mouse model with hepatoprotective effects: A prevention study; J. Ethnopharmacol. 2006; 105: 380-386.
8. M. Jesupillai, M. Palanivelu, V. Rajamanickam and S. Sathyanarayanan. Anticonvulsant effect of *Erythrina indica* lam. Pharmacologyonline 2008; 3:744-747
9. Kumar S. et al. Pharmacological evaluation of bioactive principle of *Turnera aphrodisiaca*. Indian J. Pharm. Sci.2008; 70 (6): 740-744.
10. Manigauha A., Patel S., Monga J. and Ali H. Evaluation of anticonvulsant activity of *Pongamia pinnata Linn.* in experimental animals, International Journal of Pharma. Tech. Research 2009; Vol. I (4): 1119-1121.
11. Thirupathi K., Thirupathi D. R., Krishna B. et al. Anticonvulsant Activity of Pericarpium Extract of *Balanites Roxburghii Planch* in Mice. Pharmacologyonline 2009; 1**:**1150-1157.
12. Kulkarni S. K. Handbook of Experimental Pharmacology. Vallabh Prakashan,New Delhi, 2nd ed., 1993:82-87p.
13. McDonald R. I. and Kelly K. M. Antiepileptic drugs: Mechanisms of action. Epilepsia 1993; 34: S1-8-20.
14. Ramanjaneyulu R. and Ticku M. K. Interactions of pentamethylenetetrazole and tetrazole analogues with thepicrotoxinin site of the benzodiazepine-GABA receptor ionophore complex. Eur.J.Pharmacol. 1984; 98**:** 337-345.
15. Loscher W. and Schmidt D. Which animal's models should be used in the search for new antileptic drugs? A proposal based on experimental and clinical consideration. Epilepsy Res.1988; 2**:** 145-181.