WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.074
Volume 7, Issue 19, 1082-1089. Research Article ISSN 2277– 7105

ANTICONVULSANT ACTIVITY OF AQUEOUS EXTRACT OF *TRIDAX PROCUMBENS LINN* LEAVES AGAINST MES INDUCED CONVULSIONS

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Article Received on
02 October 2018,

Revised on 23 October 2018,
Accepted on 13 Nov. 2018

DOI: 10.20959/wjpr201819-13760

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ABSTRACT

The plant *Tridax Procumbens L.* belonging to the family Asteraceae is popularly known as Coatbuttons – Mexican Daisy in English, Gavpattha in Hindi, and Dagdipala in Marathi. The chemical constituents present are alkaloids, carotenoids, flavonoids (catechins and flavones), saponins and tannins. Mineral composition present in leaves is calcium, magnesium, potassium, sodium, and selenium. Leaf mainly contains crude proteins 26%, crude fiber 17% soluble carbohydrates 39% calcium oxide 5%, Luteolin, glucoluteolin, quercetin, and isoquercetin. Whereas the oleanolic acid, fumeric acid, β-sitosterol, and tannin is present in good amounts. In recent years, the medicinal properties of plants have been investigated in the light of scientific developments throughout the world, due to their potent pharmacological activities, low toxicity, and economic viability15. Hence, the present study was designed to verify the anticonvulsant effect of aqueous extract of *Tridax Procumbens L.* in experimental animals. The aqueous extract of *Tridax procumbens Linn* was extracted by Percolation method. Phenytoin 25 mg/kg body weight used as the standard drug and different dose of aqueous extract of *Tridax Procumbens L.* are used to evaluate its anticonvulsant activity on MES induced convulsion model. In the present study Phenytoin significantly ($p<0.001$) inhibited the convulsions (i.e. flexion, extension, clonus, stupor) due to maximal electroshock. *Tridax procumbens* 4.2, 8.4 and 12.6 mg/kg (i.p.) fail to inhibit the extension and the time to recover from MES. Thus the

observations emanated in the present study indicated that the *Tridax procumbens* was not effective against MES. Lack of activity against MES induced seizures suggest that *Tridax procumbens* is not useful in suppressing generalized tonic-clonic seizures.

KEYWORDS: Anticonvulsant effect, *Tridax Procumbens Linn*, MES induced convulsion, Phenytoin.

INTRODUCTION

Epilepsy is a major neurological disorder characterized by the occurrence of recurrent seizures. Epilepsy is the second most common and frequently encountered neurological condition that imposes the heavy burden on individuals, families, and also on healthcare systems. As per a recent study, 70 million people have epilepsy worldwide and nearly 90% of them are found in developing regions.[1,2] This chronic disorder involves alterations in the voltage-dependent ion channels, reduction in inhibitory, i.e. GABA-mediated drive or increase in excitatory, i.e. glutamate-mediated inputs.[3] Antiepileptic drugs (AEDs) currently in use notably Phenytoin, Carbamazepine, Phenobarbital, and Valproate, referred to as older AEDs were (drugs introduced before 1990). These drugs induce hepatic microsomal enzymes, cytochrome P450 (CYPs) thereby complicating the use of multiple anti-convulsion drugs as well as impacting the metabolism of oral contraceptives, warfarin, and many other drugs. The drugs also enhance the metabolism of endogenous compounds including gonadal steroids and vitamin D.[4] Moreover the conventional drug therapy is associated with a lot of side effects, chronic toxic effects, and teratogenicity.[5]

The plant *Tridax Procumbens L*. belonging to the family Asteraceae is popularly known as Coatbuttons – Mexican Daisy in English, Gavpattha in Hindi, and Dagdipala in Marathi. The chemical constituents present are alkaloids, carotenoids, flavonoids (catechins and flavones), saponins and tannins. Mineral composition present in leaves is calcium, magnesium, potassium, sodium, and selenium. Leaf mainly contains crude proteins 26%, crude fiber 17% soluble carbohydrates 39% calcium oxide 5%, Luteolin, glucoluteolin, quercetin, and isoquercetin. Whereas the oleanolic acid, fumaric acid, β-sitosterol, and tannin is present in good amounts. Tridax Procumbens is known for several potential therapeutic activities like anti-inflammatory.[6] Immunomodulatory,[7] Anti-diabetic,[8] antiviral, antibiotic efficacies,[9] antiparasitic,[10] Antiobesity,[11] Anticancer,[12] wound healing and antioxidant activity,[13] Some reports from tribal areas in India state that the leaf juice can be used to cure fresh wounds, to stop bleeding, as a hair tonic. In southern Orissa, a paste prepared from the whole

plant is taken orally to relieve diarrhea. A fine paste of the leaves is applied externally to reduce swelling of hemorrhoids by the Urash in southern Bihar,[14] In recent years, the medicinal properties of plants have been investigated in the light of scientific developments throughout the world, due to their potent pharmacological activities, low toxicity, and economic viability,[15] Hence, the present study was designed to verify the anticonvulsant effect of aqueous extract of *Tridax Procumbens L*. in experimental animals.

MATERIALS AND METHODS

Tridax procumbens leaves were collected from the campus of the college in a month of June and July and shade dried. A plant was identified Agharkar institute of Pune. Piracetam UCB India Ltd, India, Diazepam, Ranbaxy India, Phenytoin, Zydus Pharmaceuticals. All drugs were dissolved and /or diluted with distilled water (vehicle). *Tridax procumbens* was dissolved in distilled water and administered intraperitoneally.

Animals: Male/ Female albino mice weighing 20-25 g and male/ female albino rats weighing 180- 250 g were obtained from National Institute of Toxicology, Pune. Animals were housed in groups of five per cage under standard laboratory conditions with food and water continuously available. A 12 h: 12 h (light: dark) cycle was used with the light on from 7:00 to 19:00 h. All behavioral testing was done during the daylight period between 10:00 and 17:00 h. Animals were tail marked and handled daily for 5 min during the last 3 days before the experiment.

Extraction[16] The aqueous extract of *Tridax procumbens Linn* was extracted by Percolation method. Moisten 1kg powdered leaves of Tridax procumbens with a sufficient amount of the prescribed menstrum (solvent). After 24 hours lower orifice is opened and menstrum is collected with a controlled speed until ¾ of menstrum is collected. Then more menstrum is added and collected from the lower orifice so that marc does not become dry. Then Marc is pressed to get extract which is combined with previous liquid. Then it is allowed to stand and then it is filtered. Recover the menstrum from the remainder of the percolate and concentrate to a soft extract in a vacuum apparatus at a temperature not exceed 45^0C.

Motor Activity[17,18] The mice were divided into four groups of five mice each. Mice were first individually placed in the photoactometer and normal movement recorded. After five minutes, the counter was stopped and the reading noted. The animal was then removed and the counter reset to zero. The same procedure was repeated for all animals.

Group 1 received Diazepam 3mg/kg, body weight Intraperitoneally.

Group 2, 3, 4 received an aqueous extract of *Tridax procumbens* 4.2, 8.4, 12.6 mg/kg body weight intraperitoneally. The animals were then individually placed in the photoactometer and the readings were noted. The results were tabulated and converted into percentages for convenient calculations.

Maximal Electroshock (MES) - Induced Convulsion in Rats[17,19] Albino rats of 150-200 g body weight were divided into five groups of five animals each. The first group, which received saline orally, served as the control whilst the second group received 25 mg/kg of phenytoin intraperitoneal (ip), and Group 3, 4, 5 received an aqueous extract of *Tridax procumbens* 4.2, 8.4, 12.6 mg/kg body weight intraperitoneally. After an hour of treatment, convulsions were produced in rats using an "Inco" convulsiometer by delivering current of 150 mA through corneal electrodes for a period of 0.2 seconds. The severity of convulsions was assessed by the duration of flexion, extension, clonus, stupor and recovery phase for each animal. Inhibition of the extensor phase was studied in this model.

Statistical Analysis and Calculations

The % inhibition (or decrement) was calculated by using the formula

% inhibition = (1-test reading/ Control reading) x 100

Student's t-test was performed for statistical analysis. $P<0.05$ was considered statistically significant.

RESULT AND DISCUSSION

Most of the drugs acting on central nervous system influence the locomotor activities in man and animals. The CNS stimulant drugs such as caffeine, amphetamine increase the locomotor activity while CNS depressant drugs such as barbiturates and alcohol reduce the locomotor activity.[20] In actophotometer, preliminary attempts were made to assess the stimulant or depressant effect of Tridax procumbens. In the present study Diazepam, *Tridax procumbens* 4.2, 8.4 and 12.6 mg/kg (i.p.) significantly ($p<0.001$) decreases the locomotor activity. (Table 1).

Epilepsy implies a periodic recurrence of seizures with or without convulsions. A seizure results from an excessive discharge of cortical neurons and is characterized by changes in electrical activity as measured by the electroencephalogram (EEG). A convulsion implies

violent, involuntary contraction(s) of the voluntary muscles.[21] Electrical stimulation of the brain of mice through corneal electrode brings about convulsions. Any convulsion whether due to some diseased process or brought about experimentally in animals has its origin in the neurons of CNS. Neurohumoral substances like acetylcholine, adrenaline, noradrenaline, serotonin, and others have been known to affect the excitability of central neurons.[22] An imbalance between the excitatory and inhibitory neurotransmitters is responsible for seizures. At the neuronal level, seizures activity often occurs when glutamatergic excitatory neurotransmitters override GABA mediated inhibiton.[23]

Table 1: Assessment of loco motor activity of aqueous extract of *Tridax procumbens Linn* (TP) using a photoactometer.

Group	Treatment (mg/kg)	Locomotor Activity		Percentage decrease of locomotor activity
		Before	After	
1	Control	813.6±1.93	789.3±2.23	2.986
1	Diazepam (3)	916.6±1.96	301.8±3.30***	67.073
2	TP (4.2)	1023.6±8.84	426.2±3.99***	58.396
3	T.P (8.4)	966.6±2.70	461.6 ± 3.14***	52.24
4	TP (12.6)	985.2±2.55	240 ± 3.80***	75.654

n=5, *p<0.5, **p<0.01, ***p<0.001 compared vs control. (ANOVA followed by Tukey Kramer multiple comparison test).

Table 02: Effect of aqueous extract of *Tridax procumbens Linn* (TP) on maximum electric shock induced flexion, extension, clonus, stupor, and recovery/ death

Treatment (mg/kg)	Time (sec) in various phases of convulsions				
	Flexion	Extension	Clonus	Stupor	Recovery/Death
Control	1.58±0.08	8.92 ± 0.32	1±0	13±0.70	44.6±1.31
Phenytoin (25)	1.02±0.01***	4.38±0.25***	0.60±0.04	0	14.45±0.50***
TP (4.2)	1.72±0.04	13.65±0.50***	3±0.54*	22.4±1.63*	138.8±7.65***
TP (8.4)	1.59±0.01	16.15±0.51***	1.73±0.19	13.2±0.58	174.4±5.21***
TP (12.6)	1.38±0.03	16.09±0.89***	3.4±0.74**	21.8±1.15	116.6±2.31***

n=5, *p<0.5, **p<0.01, ***p<0.001 compared vs control. (ANOVA followed by Tukey Kramer multiple comparison test).

Several animal models of convulsions have been developed to evaluate anti-seizures activity. Many drugs that increase the brain contents of GABA have exhibited anticonvulsant activity against seizures induced by Maximum Electro Shock (MES), Pentylenetetrazol (PTZ) and Lithium- pilocarpine (Li-Pilo). MES test predicts activity against generalized tonic-clonic and cortical focal seizures and the PTZ test against absence seizure, while Lithium-pilocarpine was found useful in status epilepticus.[24] The MES model has served to identify antiepileptic

drugs that are functionally similar to phenytoin.[25] Seizure of MES can be blocked either by inhibiting the voltage-dependent Na+ channels or by blocking glutamatergic excitation mediated by the N-methyl-D-aspartate (NMDA) receptors.[26]

In the present study Phenytoin significantly ($p<0.001$) inhibited the convulsions (i.e. flexion, extension, clonus, stupor) due to maximal electroshock. *Tridax procumbens* 4.2, 8.4 and 12.6 mg/kg (i.p.) fail to inhibit the extension and the time to recover from MES **(Table 02).** Thus the observations emanated in the present study indicated that the Tridax procumbens was not effective against MES. Lack of activity against MES induced seizures suggest that *Tridax procumbens* is not useful in suppressing generalized tonic-clonic seizures.

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