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HALOPHYTIC PLANT EXTRACTS AS A PROMISING SOURCE OF ANTIEPILEPTIC AGENTS- A PRE-CLINICAL STUDY ON PTZ-INDUCED SEIZURES IN ALBINO WISTAR RATS

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ABSTRACT
Medicinal plants have been used as potential sources for new drug compounds. Halophytes have been used traditionally to cure a range of diseases. This study explores the anticonvulsant activity of medicinal halophytes against pentylenetetrazol (PTZ) induced seizures in Albino Wistar Rats. The antioxidant activity and phytochemical contents of medicinal halophytes were also determined. The ethanolic extracts (1000mg/kg body weight) of 12 medicinal halophytes were used. No mortality and signs of toxicity were evident in any of the halophytic extracts tested. A significant increase in latency (3-23 folds) as well as decrease in duration of myoclonic tonic clonic convulsions including flexion time (13-68%), extension time (3-55%), tonic clonic time (43-85%), stupor duration (30-59%) and frequency of convulsions (40-77%) were observed in halophyte treated group as compared to control. Halophytes showed strong DPPH radical scavenging activity (29.56% to 84.25%) with high contents of total polyphenols (19.54 to 57.19 mg GAE/g). Interestingly, halophytes with higher content and activity of antioxidant compounds showed maximum anticonvulsant effects, which were comparable to or even better than the positive control (Dizapam). This study reports the antiepileptic potential of antioxidant-rich halophytes and provides better insights towards the drug development. It also paves the road for complementary medical therapies against seizures and other similar neurological issues.

Key Words: Anticonvulsant activity, Bioactive compounds, Drug discovery, Natural products, Neurological effects, Phytochemicals

1. INTRODUCTION
Epileptology branch of Neurology was coined by William P. Spratling in the early 20th century (1). Epilepsy is a medical disorder that has been documented since 4000 BC. It is a neurological condition that is not communicable and is brought on by a large quantity of brain cells (neurons) undergoing excessive electrical discharges. Seizures are involuntary movements of the part of body (partial) or the entire body (generalized) with/without consciousness, are what identify epilepsy as a chronic brain illness. Recurrent episodes of epilepsy that may involve seizures, sensory disturbances, and abnormal conduct make up its hallmark features (2). So, the symptoms of epilepsy might range from a slight break in concentration (attention) or muscular twitches to a severe and protracted uncontrollable movement. Epilepsy's toll is not yet fully assessed and understood as the likelihood of having a seizure varies with age and region (3). The highest occurrence rates were observed in under

20 and over 65 years aged people. In majority of cases (75%), the disease begins before the age of 20 and it's most prevalent type observed is generalized seizures (4). Epilepsy is a global health problem affecting approximately 50 million people worldwide. It is one of the most common chronic neurological diseases in the world with serious physical, economic and discriminatory consequences in some parts of the world. Epilepsy is estimated to affect almost 10 out of every 1000 people in Pakistan. The treatment of disease includes several drugs mainly obtained from medicinal plants that used in their pure form or modified to semisynthetic drug. The drug discover through natural product research has been fruitful over the years. Traditionally, there are several plant species like halophytes that are significant in the treatment of epilepsy and other neurological diseases.

Halophytes are salt tolerant or salt resistant plants that grows in soils or waters of high salinity and have remarkable ability to complete their life cycle in saline conditions. To grow in highly salinized habitats, they have evolved a variety of morphological, anatomical, and ecophysiological adaptations and techniques (5,6). On seashores, in estuaries, in saline seeps and flats, halophytes have a wide range of potential uses as food, fodder, fiber, fuel, medicine and other goods (7,8). Halophytes can also be employed in phytoremediation to examine or quantify the salinity levels of nearby soils since they can store and absorb salt ions as well as other rare-earth elements (5). Halophytes have long been utilized in traditional medicine (9). It is well known that a number of these plants are effective in treating conditions like high blood pressure, diabetes, skin conditions, digestive problems, heart conditions, arthritis, and abnormalities of the urinary tract (10). Others have sedative and antipyretic properties. These plants contain a few known and categorized chemical compounds. Local plant medicine is widely used, and there are numerous specialized institutes that study it.

In this study various halophytes from different plant families including, Amaranthaceae (*Aerva javanica, Arthrocnemum macrostachyum, Suaeda fruticosa*), Acanthaceae (*Avicennia marina*), Apocynaceae (*Calotropis procera*), Convolvulaceae (*Cressa cretica, Ipomea pes-caprae*), Boraginaceae (*Heliotropium bacciferum*), Fabaceae / Leguminosae (*Prosopis cineraria*), Salvadoraceae (*Salvadora persica*), Malvaceae (*Thespesia populnea*) and Molluginaceae (*Glinus lotoides*) are taken, of which some of them may or may not have previously reported potential for any neurological activity. This study majorly focuses on the screening of the above-mentioned plants to rule out which halophyte have possible future anticonvulsant activity to be used as medicine with of course after multiple clinical trials. The antioxidant activity and total phenolic content of medicinal halophytes were also analyzed.

2. METHODOLOGY

2.1. Sample collection and preparation

Aerial parts of halophytic plants have been harvested from their natural populations and dried in shade. Dried plant material was ground using mechanical grinder and was subsequently transformed into a fine powder using a Ball Mill (Retsch MM-400). Plant material was thrice extracted in ethanol, each for 24 hrs, using a shaking water bath (GFL-1092). The filtered supernatants of each plant were then combined and concentrated using a rotary evaporator (Buchi) and stored in the refrigerator until use (11).

2.2. Antioxidant Activity and Total Phenolic Content of Medicinal Halophytes

2.2.1. DPPH Radical Scavenging Activity

Following Brand-Williams Assay, antioxidant efficacy of medicinal plant extracts was analyzed against 1, 1-Diphenyl-2-picrylhydrazyl (DPPH) radical (12). Different dilutions of extract were mixed with DPPH reagent (1:1) and were kept in the dark at room temperature. After 30 min, the absorbance was measured at 515 nm. The scavenging activity of DPPH radical was measured as percentage inhibition which then used to find out IC_{50} value (extract concentration that induced a 50% inhibition of DPPH radicals) of each plant extract.

2.2.2. Total Phenolic Content

Folin-Ciocalteu colorimetric analysis was performed to determine the total phenolic content (38). Folin-Ciocalteu reagents (0.2 N) was used to oxidize the samples, and saturated sodium carbonate (75 g/L) was used to neutralize the reaction (16). After incubation for 2 hours at room temperature, absorbance was measured by using an UV/Vis spectrophotometer (Beckman Coulter DU530) at 760 nm by using Gallic acid to create a standard curve.

2.3. In-Vito Anti-Convulsant Activity

2.3.1. Experimental Animals

Wistar rats (which weighs 180–200 g) kept or acclimated in the animal home under controlled lighting and temperature (12 hr light/dark cycles, at 21 °C), with access to ad libitum laboratory food and water. Ethical clearance was taken from Institutional Bioethical Committee (IBC), University of Karachi (IBC KU-188/2021) prior to experimentation.

2.3.2. Screening Procedure

After acclimatization of Rats for one week, they were subjected to convulsion tests against the crude extracts. There were 12 plant extracts, 60 animals were obtained, five animals for each plant extract. The screening dose for crude extract was 1000mg/kg body weight of rats dissolved in saline and administered orally. After 15-30 mins of administrating crude extract, PTZ dose of 80-85mg/kg body weight of rats was made in saline and injected intraperitoneally (I.P.).

2.3.3. Convulsion Tests

Following the PTZ injection (I.P.), the animals were subjected to convulsion tests and observed for 30-40 mins. The parameters that were noticed during the test were latency (time period for seizure onset after PTZ injection), tonic-clonic convulsions and their frequency, flexion and extension of limbs during seizure and stupor (20). The tests were video recorded and later above parameters were analyzed and reported.

3. RESULTS

3.1. Antioxidant Activity and Total Phenolic Content of Medicinal Halophytes

The description of medicinal halophytes used in this study with previously reported relevant medicinal effects/ traditional uses is summarized in Table 1. In this study the ethanolic extracts of halophyte plants showed that all plant species contain bioactive polyphenols (mg GAE/ g extract) ranged between 19.54 to 57.19 (Fig. 1). The higher TPC values were found in *I. pes-caprae* (57.19), *S. fruticosa* (49.19), *A. javanica* (33.99) and *A. marina* (31.18). While the *P. cineraria* showed the lowest TPC content (19.54).

Ethanolic extracts of all halophytes shows the strong antioxidant activity (Fig. 2). The DPPH radical scavenging activity was ranged from 29.56% to 84.25%. The most prominent species of halophytes that showed high DPPH activity includes *I. pes-caprae* (84.25%), *S. fruticosa* (78.74), *A. javanica* (75.25%) and *A. marina* (62.17%). While the *P. cineraria* showed the lowest DPPH inhibition (29.56%).

A strong positive correlation ($r^2 = 0.808$) between DPPH activity and TPC of halophyte extracts was observed (Fig. 3).

3.2. Acute Toxicity Study

No mortality was seen at a dose of 1000 mg/kg for the study period of 14 days. However, no changes in activity like scratching, curved tail, shivering, grooming, excitation, convulsion, fatigue, diarrhoea and falling of hair has been observed.

3.3. Assessment of Pentylenetetrazole (PTZ) Induced Seizures

This research targets the twelve halophytes with beneficial medicinal properties including, *A. javanica, A. macrostachyum, A. marina, C. procera, C. cretica, G. lotoides, H. bacciferum, I. pes-caprae, P. cineraria, S. persica, S. fruticosa, T. populnea*. All the extracts showed the protection against convulsing effects of PTZ induced seizures in experimental rats. Ethanolic extracts (1000 mg/kg, p. o.) reduced the total duration of generalized tonic and clonic seizure, thereby influenced on the latency, duration and frequency of tonic generalized extensor and clonic seizure when compared with vehicle control. However, *A. macrostachyum* (943.3±30.32) (23%), *A. javanica* (865.3± 23.5) (21%), *S. fruticosa* (662.3±17.1) (15%) and *I. pes-caprae* (640±23.1) (16%) significantly increased the latency of generalized clonic seizures as compared to control (976±15.6) and placebo groups (41.3±3.5) (Fig. 4, Table 2). Similary, *G. lotoides* (391±18.19), *T. populnea* (352.3±21.10), *S. persica* (312.3±18.2), *C. cretica* (196.6±14.52), *C. procera* (186.0±16.07), *H. bacciferum* (155±8.7), *P. cineraria* (134.6±12.4) and *A. marina* (121.6±7.26) were also showed the increase in latency when compared with negative control group (Table 2). The epileptic spasm was characterized by sudden sustained extension and flexion of limbs or/and trunk. A significant difference in tonic flexion time was found between extract treated group and control group. *I. pescaprae* (33.3±6.6) (68%), *A. macrostachyum* (38.3±7.2) (63%), *A. javanica* (39.6±5.4) (62%) and *S. fruticosa* (56.0±4.9) (46%) were most prominent among others. The duration of hind limb extension also observed to be decreased significantly when compared with control groups i.e. *A. javanica* (32.33±3.4) (55%), *H. bacciferum* (36.33±2.4)(50%), *I. pes-caprae* (42.3±4.9) (41%), *A. macrostachyum* (46±2.08) (36%), *S. fruticosa* (49±2.08) (32%), *G. lotoides* (50±2.8) (31%), *P. cineraria* (66±6.6) (9%), *C. procera* (66±2.08) (9%), *S. persica* (67.33±5.04) (7%), *A. marina* (68±6.4) (6%), *T. populnea* (69.6±3.75) (4%), *C. cretica* (86.33±5.54) (3%) (Fig 4; Table 2). However, the tonic clonic mean duration decreased of *A. macrostachyum* (46.0±2.08) (85%), *A. javanica* (32.3±3.4801) (84%), *I. pes-caprae* (42.3±4.9) (82%) and *H. bacciferum* (36.3±2.4) (78%) was also significantly different with control group. The stupor has been observed at the end of tonic clonic seizures and treatment with extracts showed significant decrease in duration of stupor *A. javanica* (310±8.08) (59%), *A. macrostachyum* (52%), *I. pes-caprae* (314.6±8.1) (59%), *S. fruticosa* (336.6±18.5) (56%) and *A. marina* (349.6±10.4) (54%) as compared to vehicle control. The frequency of seizures declined significantly in given extract treatment groups *A. macrostachyum* (1.0±0.0) (77%), *S. fruticosa* (1.33±0.3) (70%), *A. javanica* (1.3±0.3) (70%), *I. pes-caprae* (1.33±0.3) (70%), *C. cretica* (1.6±0.3)(63%) and *S. persica* (2±0.6)(53%) (Fig 4; Table 2). One-way ANNOVA and Dennett's test was led to test significant comparison of tested and control groups. Animals treated with twelve extracts produced significant increase in latency of seizures in relation to control group. The similar delayed onset convulsions were observed for the diazepam treated animals.

4. DISCUSSION

The present study conducted to screen out the halophytic plants which have already reported some medicinal properties, more specifically with the potential effects on central nervous system (CNS) and anticonvulsant activities (21). Medicinal plants and their bioactive compounds are essential natural resources and have been used since centuries for treatment of various human aliments (10) but sometimes they pose potential hazards for human health (18). In this study, such toxicity effects were tested on experimental rats treated with various plants extracts before assessing their potential antiepileptic activity. The acute toxicity study suggests that ethanolic extracts are safe as LD_{50} value of oral dose of 1000 mg/kg by the oral route are low toxic (22). At the relatively high doses used 1000 mg/kg, no mortality has been reported. With the use of herbs and synthetic compound the changes in body weight and water and food consumption considered as an indictor for adverse effects of chemicals (23). In this study, there was non-significant change in body weight of extract treated animals compared to the control group representing absence of adverse effects. However, no changes in activity like scratching, curved tail, shivering, grooming, excitation, convulsion, fatigue, diarrhea and falling of hair has been observed.

Pentylenetetrazole (PTZ)-induced seizures is the most extensively used method of acute seizures and study of development of AEDs. PTZ leads to induction of convulsions by blocking the GABA-mediated Cl^- influx in animals (24). The results of the following study demonstrated the halophytic plants possess the anticonvulsant activity by significantly delaying the latency time of seizures. Furthermore, theses extract also showed the great reduction in frequency and duration of tonic clonic seizures. These efficacious outcomes of ethanolic extracts suggest their potential in enhancing GABAergic neurotransmission (25). The extracts of *A. javanica, A. macrostachyum, I. pes-caprae* and *S. fruticosa* showed the maximal protection against PTZ induced seizures (Fig. 4, Table 2). Halophytes possess certain phytochemicals that could potentially inhibits the deleterious effects of chemoconvulsants by increasing the latency, decreasing the duration and frequency of seizures. These phytochemicals such as phenols, flavonoid, alkaloids and tannins and their combined effects could hinder the abnormal electrical firing in neurons and may interact with ion channels in the brain and hence delay the seizures. *A. javinaca* contain high content of flavonoids and tannins and found to possess strong antioxidant activity, thereby greatly increased the GABA receptor hence provide neuroprotection and depressive like behavior in experimental mice (26). The probable mechanism of these phytoconstitiuents could be modulating the activity of GABA/glutamate receptor activity, purinergic transmission, cholinergic pathways and ATPases catalytic function. The major flavonoids found in *A. javanica*, kaempferol and kaempferol-3-O-glucoside derivatives, are promising natural neuroprotective agents with reported antioxidant, antiinflammatory, and TNF-α level reducing activities (27). In addition, kaempferol develop the variety of responses that improves the mitochondrial mechanisms thus reduce oxidative stress, inhibit activity of acetyl cholinesterase and displayed anti-depressant effects (27).

A. macrostachyum- a potential halophytic herbs contain high quantity of phytochemicals, intermediate and secondary compounds, phenols and flavonoids and fatty acids and its esters, contribute to their natural antioxidant and reducing activities (28). The plant found to be rich in phenolic compounds and possess radical scavenging and reducing potential abilities (8). It produces enzymes responsible for lipid peroxidation and thus allows reduction of hydroxyl radical production (29). *A. macrostachyum* contains large quantities of polyunsaturated fatty acids (α-linolenic and linoleic acids), ingresorcinol, kaempferol, quercetin alkaloids and phenols, flavonoids and phlorotannins (28). Some of these compounds possess sedative, anxiolytic or anticonvulsant effects via modulating the BZD-site of $GABA_A$ receptors (30). Quercetin reduce kainic acid-induced seizures by downregulation of GABA gene expression (31). Similarly, kaempferol (KPF) has proved to be neuroprotective through activation of various neuro-proinflamatory pathways such as NF-kB, p38MAPK, AKT, and β-catenin cascade (32). Kaempferol and flavonoids showed reversal of multidrug resistance against epilepsy by inhibiting the accumulation of glycoprotein P (gp-P) encoded by MDR1 gene in brain astrocytes, however, the mechanism of gd-P inhibition is not clearly understood (33). Antioxidant ability of *S. fruticosa* directly correlated with the phenols, flavonoids, carotenoids, and triterpenes that exerts their actions by scavenging reactive oxygen species, which prevent potential damage to cellular components (8,11,34). Flavonoids and phenols greatly increased the lipid peroxidation by increasing the mitochondrial MDA level and thus reverse the impaired oxidative stress (35). *Ipomea pes-caprae* contains anthocyanins, phenols, coumarins, leucoanthocyanins, quinones, alkaloids, flavonoids, tannin phlobatanins, saponins, steroids, cardiac glycosides, triterpenes, quercetin 6"-O-glucoside, quercetin 3'-O-galactoside, and quercetin 3'-O-glucoside (36, 37). The phytochemical analysis of Ipomoea also revealed the occurrence of saponins and flavonoids that are profoundly attributed to the anticonvulsant activity (38). Flavonoid compounds can interact and bind with two or more active sites on GABAA receptors and act as agonist at the gate receptor even without release of GABA (39) and produce benzodiazepines like actions (40). In another study, *Ipomea asarifolia* reported to have anti-convulsant activity via GABAergic, glutaminergic and opiodergic pathways in PTZ-induced seizures (41). *Cressa cretica* contains phytochemicals including, tricontanoic acid, stigmasterol, kampferol-3-O-glucoside, kampferol-3-O-rhamnoglucoside, beta-amyrin, cresoside, quercetin, quercetin-3-O-glucoside, rutin,

cressatriterpenic acids, cressanyl ester and chlorogenic acids (41-43). It is a potent candidate for Alzheimer's disease and Memory deficits due to its memory and learning enhancing effects (41,44). It lowers overall MDA and NO levels as well as acetylcholinesterase activity throughout the brain, which suggest anticonvulsant potential of this plant apart from its other effects on CNS. Similarly, *P. cineraria* contains carbohydrates, proteins, tannins, flavonoids, cardiac glycosides, alkaloids, terpenes, and steroids (45-46). Additionally, it has been shown to have dose-dependent anticonvulsant effect against maximal electroshock produced seizures (MES) and PTZ (47). *S. persica* (Linn.) contains a variety of phytochemicals including salvadoricine, salvadoside, indole alkaloids, benzyl nitrile, eugenol, eucalyptol, stigmasterol, butanediamide etc. Seizures brought on by PTZ have also been experimentally treated with decoction of this plant and it also possess neuroprotective and antiviral effects (48-49).

5. Conclusions

The phytoconstitiuents of halophytic plants are found to more effective natural source of antiepileptic treatment due to the presence of various phytoconstitiuents that exhibited a higher antioxidant activity. However, the plant extract should be used for fractionation and isolation of the active constituents to determine the possible mechanism of action. It is concluded that research like this not just paves the road towards execution but also provides the door for complementary medical therapies for conditions like seizures and other similar neurological or psychiatric issues, which were long believed to be incurable. Additionally, it is hoped that this research would benefit and make a positive impact on the field of phytotherapy research in the future.

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Declaration of interest

The authors declare that they have nothing to disclose.

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Table 1. Activity and uses of medicinal halophytes for brain disorders and comorbidities.

Family & Species	Part	Epilepsy Induction	Extract	Doses (mg/kg)	Disorders	References
Avicenniaceae						
Avicennia marina	L, FR	PTZ	M	200-400	Dementia, Alzheimer's	50
Amaranthaceae						
Aerva javanica	L	-	M	100-500	Depression & Neuroinflammation, anticholinesterase activity	26
Arthrocnemum macrostachyum	-	-	M	-	Anticholinesterase activity, neurodegenerative diseases.	29
Suaeda fruticosa	-	-	-	-	Ophthalmia	11
Apocynaceae						
Calotropis procera	R,L	LIT, MES, PTZ, PIL, PIC	E,CH,A	50-500	Depressant, analgesic	51
Boraginaceae						
Heliotropium bacciferum					Alzheimer's, Stroke	52
Convolvulaceae						
Cressa cretica	Whole plant	-	EE	200-400	Alzeihmer's, amnesia, nootropic activity	42-45
Ipomea pes-caprae	L,S,F	-	ME	-	Hallucinogenic, antinociceptive, analgesic	37-39
Fabaceae / Leguminosae						
Prosopis cineraria	ST	PTZ	M	200-400	Depression, anxiety, neurological impairment	47-49
Malvaceae						
Thespesia populnea	Bark, L	MES	EE, HA	100-400	Alzeihmer's, Amnesia, convulsion, anxiety	53-54
Molluginaceae						
Glinus lotoides	Whole plant	-	EE	100-500	Depression, muscle spasms- antispasmodic activity	55-56
Salvadoraceae						
Salvadora persica	ST, F, R	PTZ	CH, DEE, EA	500	Alzheimer's, Parkinson's, insomnia, depression	49-50

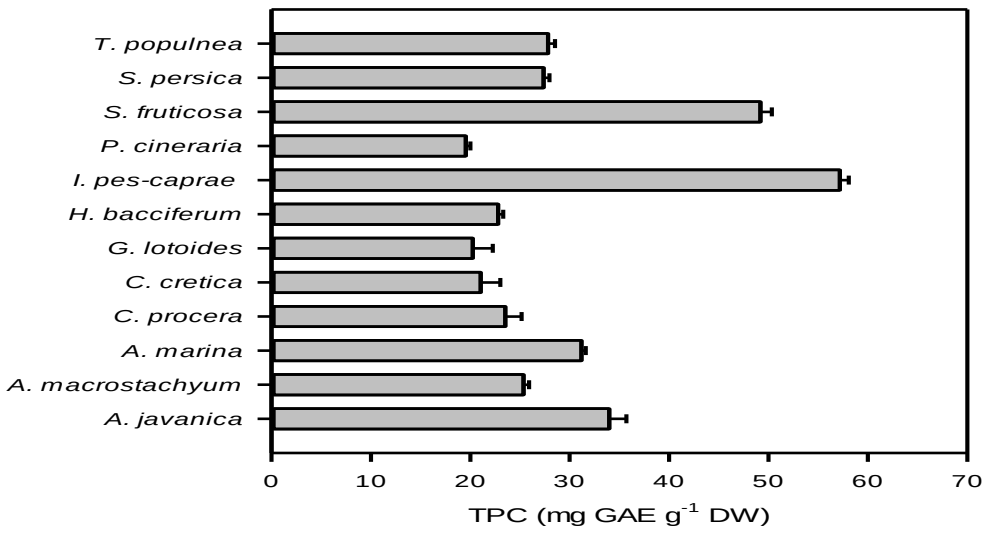

Figure 1: Total phenolic content (TPC) of medicinal halophytes.

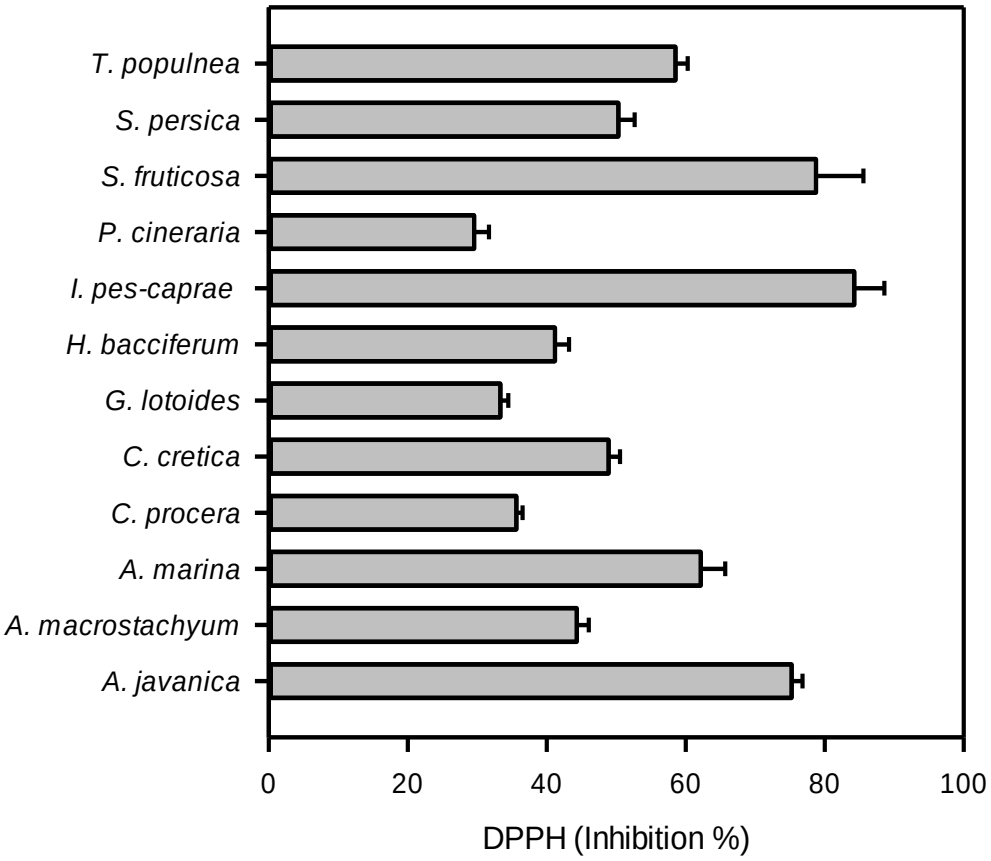

Figure 2: DPPH radical scavenging activity of medicinal halophytes.

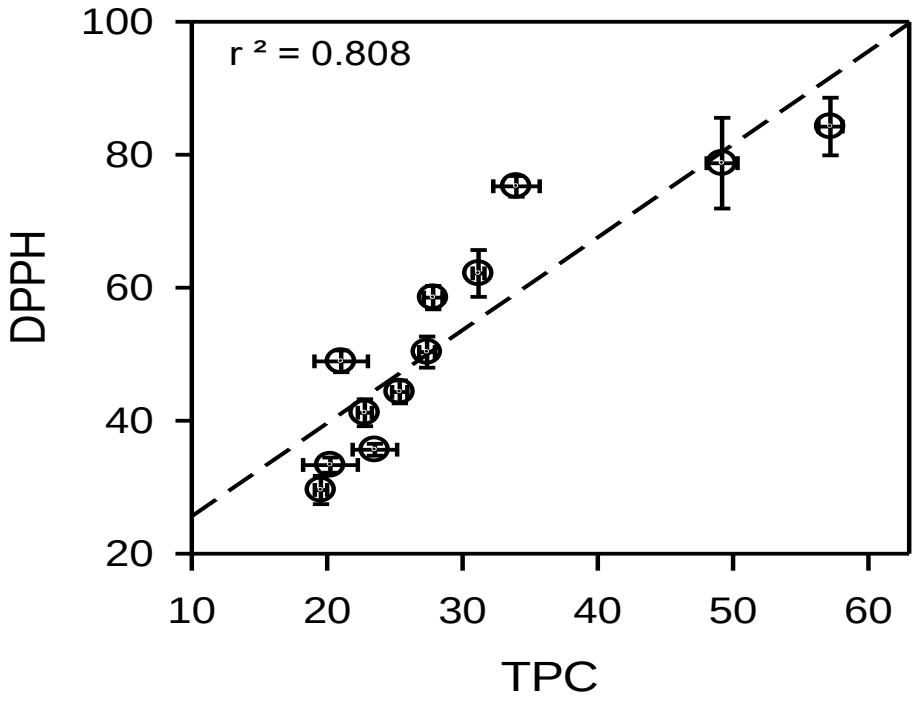

Figure 3: Regression analysis between total phenolic content (TPC) and DPPH radical scavenging activity of medicinal halophytes.

Table 2. Anticonvulsant activity of medicinal halophytes against PTZ induced rat model. Values are expressed as mean ± standard error (n=6) and different letters in superscript represents significant differences at $p < 0.05$ using LSD post-hoc test.

Treatments Groups	Latency of convulsion (s)	Whole Body Myclonic Tonic clonic convulsions (s)				Frequency of seizures
		Flexion	Extension	Tonic-clonic	Stupor	
Saline (control -ve)	41.3±3.5^{a}	103.3±3.5^{d}	72.3±3.7^{f}	647.6±7.9^{j}	766.6±24^{h}	4.3±0.3^{d}
Dizapam (control +ve)	976.0±15.6^{i}	52.3±5.4^{b,c}	57.0±7.2^{d,e}	85.3±3.7a	140.3±7.8^{a}	1.3±0.3^{a,b}
A. macrostachyum	943.3±30.3i	38.3±7.3^{a,b}	46.0±2.1^{b,c,d}	95.0±2.9^{a,b}	368.6±13.8^{c,d}	1.0±0.0^{a}
A. javanica	865.3±23.6^{h}	39.6±5.5^{a,b}	32.3±3.5^{a}	103.3±3.5^{b,c}	310.6±8.1^{b}	1.3±0.3^{a,b}
A. marina	121.6±7.3^{b}	65.0±3.6^{c}	68.0±6.4^{e,f}	139.3±3.5^{e}	349.6±10.5^{b,c}	2.3±0.3^{b,c}
C. procera	186.0±16.1d	63.3±6.0^{c}	66.0±2.1^{e,f}	346.3±4.1^{h}	434.3±11.3^{e,f}	3.6±0.3^{d}
C. cretica	196.6±14.5^{c,d}	89.6±4.2^{d}	70.3±1.5^{e,f}	125.0±3.5^{d,e}	356.6±18.6^{c}	1.6±0.3^{a,b,c}
H. bacciferum	155.0±8.7b^{c}	57.6±5.4^{c}	36.3±2.4^{a,b}	139.6±2^{e}	460.6±7.9^{f}	2.0±0^{a,b,c}
I. pes-caprae	640.0±23.1^{g}	33.3±6.6^{a}	42.33±4.9^{a,b,c}	114.0±4.6^{c,d}	314.6±8.1^{b}	1.3±0.3^{a,b}
G. lotoides	391.0±18.2^{f}	56.6±4.7^{c}	50.0±2.9^{c,d}	130.3±3.3^{e}	369.0±11.3^{c,d}	2.3±0.3^{b,c}
P. cineraria	134.6±12.5^{b}	69.6±3.8^{c}	66.0±6.7^{e,f}	369.4±3.8^{i}	527.3±8.4^{g}	2.3±0.3^{b,c}
S. persica	312.3±18.2^{e}	67.0±5.0^{c}	67.3±5.0^{e,f}	166.6±4.1^{f}	370.6±7.4^{c,d}	2.0±0.6^{a,b,c}
S. fruticosa	662.3±17.1^{g}	56.0±4.9^{c}	49.0±2.1^{b,c,d}	95.66±3.2^{a,b}	336.6±18.6^{b,c}	1.3±0.3^{a,b}
T. populnea	352.3±21.1$^{e.f}$	59.0±5.1^{c}	69.6±3.8^{e,f}	240.4±8.4^{g}	535.3±2.9^{g}	2.6±0.3^{c}

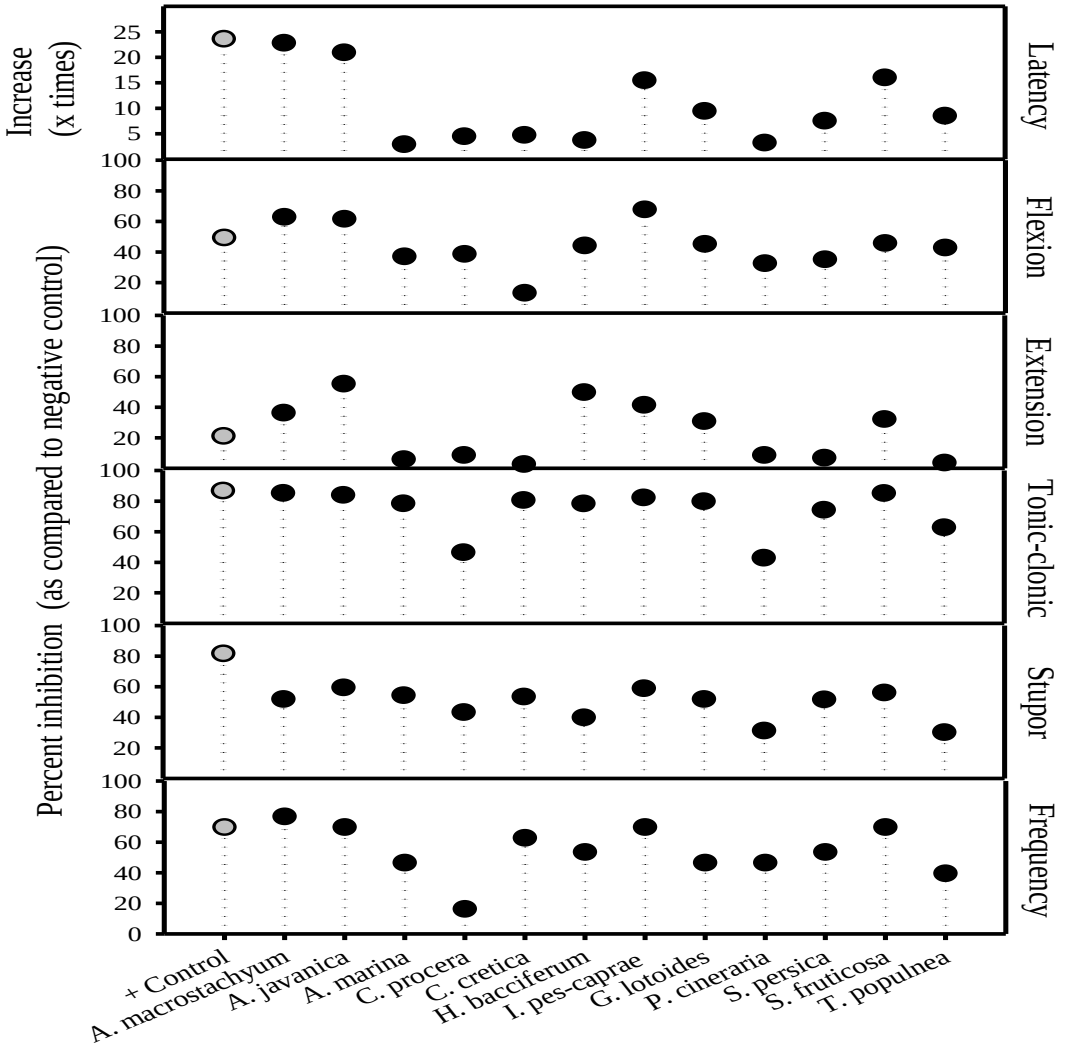

Figure 4: Effects of halophytic plant extracts on different anti-convulsant activity parameters as compared to the negative control.