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ANTICONVULSANT EFFECT OF THE HYDROALCOHOLIC EXTRACT OF AJWA DATES (PHOENIX DACTYLIFERA) IN ANIMAL MODEL

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Abstract:

Background: *Epilepsy is one of the most common serious, life threatening neurological disorder. The current modern antiepileptic drug are associated with side effects, dependency, sedation, chronic toxicity, and teratogenic effects and in approximately 30% of the patients is ineffective. Ajwa dates are used as many traditional/classical medicine for the treatment of different diseases including convulsions and seizures.*

Methods: *In this study, anticonvulsant effects of hydro alcoholic extract of Ajwa date fruit were examined by using pentylentetrazole (PTZ) model in mice. Thirty min. later to saline (10ml/kg), Ajwa date extract (200,400 mg/kg) and diazepam(1mg/kg) treatment, an i.p. dose of PTZ (90 mg/Kg) were given to all animals and each animal were observed for onset time of myoclonic jerks and tonic-clonic seizures, as well as duration of tonic-clonic seizures for 30 min via digital video camera. The animals will be also observed for mortality (% mortality = number of mice dead after convulsion/total number of mice used × 100).*

Results: *Ajwa dates extract at the doses of 200,400 mg/kg prolonged the time of onset of seizure and decreased the duration of seizures compared to control (saline) group.*

Conclusions: *It seems that Ajwa date have anticonvulsant effect and could be useful for the control and treatment of seizures. And in these effects, opioid receptors might probably be involved. More studies are needed in order to investigate its exact mechanism.*

Keywords: *Ajwa dates, Seizure, Hydroalcoholic extract.*

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INTRODUCTION:

Among many neurological disorders, epilepsy is the most serious and life threatening disorder. [1] Seizers developed due to the rapid excitation and periodic firing of brain neurotransmitter/cerebral neurons. [1] voltage gated sodium channels control the initiation of normal and seizer types action potential. [2] All age groups, generas and social groups are affected by epilepsy. roughly 50 million populations have been diagnosed with epilepsy worldwide. [2] The overall patient's quality of life is predominantly effected by epilepsy. [3] Tough, many epileptic drugs are available to inhibit seizers but no any effective prophylaxis and cure available.[3] Recent clinical study shows that none of the newly introduced 3rd generation antiepileptic drugs exhibit refine efficacy over the traditional antiepileptic drugs such as carbamazepine and valparote .[4] Diverse group of anti-epileptic drugs are prescribed by the practioners but these drugs have wide range of adverse effects including liver toxicity, ischemia, depression, cognitive disabilities and motor impirement.[9] Furthermore, many antiepileptic drugs are narrow therapeutic window drugs.[7] In spite of diverse discovery of current antiepileptic drugs into clinical practice, only 20-30% patients are managed by the available pharmacological therapy.[1] Due to this, there is a requirement of such advanced discovery of anti-epileptic drugs which have an upgrade / effective efficacy and appropriate safety profile.[4]

Herbal medicines are playing significant/foremost role in the invention of several new drugs including antiepileptic medicines. [8] Date fruits (phoenix dactyifera L) widely cultivated as an economical and food crop in the middle east, Pakistan, India and many other Arid regions of the world. There are different kinds of dates, among them Ajwa date is most popular for its significant therapeutic properties. It is cultivated specifically in the holy city of Al Madina Al- Munawwrah,KSA. [5] They are wonderful source of proteins, vitamins and energy. They also provide many useful and essential minerals, fats, high dietary fibers and sugars. They comprised numerous chemical substances like glycosides, flavonoids, sterols and polyphenols. [6] Ajwa dates use as an anti-oxidant, anti-inflammatory, hepatoprotective, nephroprotective, hypolipidemic and cardio protective. [7] Moreover, Ajwa dates are very beneficial for nursing mothers,as they are helpful in enriching the breast milk. Different studies showed that females who eat Ajwa dates on daily basis, their children are least sensitive to infections and diseases. They are rich source of iron, so are helpful in the treatment and prevention of anemia. [12]

Based on the evidences in traditional medicine and the results of a preliminary experimental trial study confirmed the anticonvulsant effects of hydro-alcoholic extract of Ajwa date fruit by using pentylentetrazole (PTZ) model in mice, or hydro-alcoholic extract has the potential to suppress the convulsions, Hence the present study was conducted to evaluate the anticonvulsant efficacy of hydro-alcoholic extract of Ajwa dates and compare its potency with the anticonvulsant effects of commercial drug.

EXPERIMENTAL:

Material and Methods

Animal: Male BALB/c mice (30-47 g) were obtained from the NIH (national institute of health). The animals were individually placed in animal house with 12/12 h light/dark cycle at 21 ± 2°C and had free access to food and water. On the day of the experiment animals were brought from the animal house. All the animals were checked to rule out any infection, injury or any other illness.

Plant Material: Ajwa dates used in the present study were fresh, ripe, medium sized, fleshy, soft, and have basal white lines on the black exocarp. Briefly, the edible part of date fruit was manually separated, and soaked in hydro-alcoholic solution i.e. 99.9% ethanol and purified water for 3 to 4 days. The mixture was then filtered and evaporated with the help of rotary evaporator to get the extract.

Chemicals: Drugs used in the study were as follows:

1. Pentylenetetrazole (induces convulsion)
2. Normal saline (Control drug)
3. Diazepam injection (Standard drug)

All chemicals were dissolved in normal saline and prepared freshly each time and administered intraperitoneally.

Anticonvulsant Assay (PTZ- Induced Seizure)

METHODOLOGY:

Animals were randomly divided into five groups of five each. It consisted of one control group, one standard group and two test groups.

[1] Control group (C): Normal saline (10

mL/Kg)

[2] Test 1 (T_1): Ajwa date's extract (200 mg/kg)

[3] Test 2 (T_2): Ajwa date's extract (400 mg/kg)

[4] Standard group (S): Diazepam (1 mg/Kg)

The animals were injected (i.p) with control drug, Ajwa date's extract (test groups) and standard drug. Thirty minutes later, an i.p. dose of Pentylentetrazole (PTZ) (90 mg/Kg) was given to all animals and each animal was observed for 30 minutes for the occurrence of the seizure and timing was maintained using the digital clock.

The following parameters were studied

a) Time of onset of the myoclonic jerks
b) Time of onset of the tonic-clonic seizures (seizure latency)
c) Duration of clonic phase of seizure for 30 minutes via digital video camera

At the end of the thirty minutes the animals were inspected for any injury or residual damage. The animals were also observed for mortality (% mortality = number of mice dead after convulsion/total number of mice used × 100).

Statistical Analysis

Statistical analyses were analyzed through one-way analysis of variance (ANOVA) using the statistical Package for Social Sciences followed by Post-hoc Turkey-Kramer's test. The p value <0.05 was considered as the level of significance. Data are presented as a line diagram for Seizure latency presentation and bar diagram was constructed using the Graph Pad Prism 5. All the values were expressed as mean ± SEM (standard error of the mean). Asterisk (*) indicates the statistical significance, with the level significance for comparison.

RESULTS:

Test groups, that significant delayed the onset of myoclonic jerks, tonic-clonic seizure and shorten the duration of tonic-clonic seizure were considered to exhibit anticonvulsant activity.

Table 1: Time of onset of the myoclonic, tonic-clonic seizure and Duration of clonic phase of seizure (seizure latency)

S.No.	Group	Seizure Latency in Seconds (Mean± SEM)		
		Time of onset of the Myoclonic Seizure	Time of onset of the Tonic-Clonic Seizure	Duration of Clonic Phase of Seizure
1	Normal saline (C)	36.45 ± 1.7	42.67 ± 1.8	40.60 ± 1.5
2	Ajwa date's extract (T_1)	75.00 ± 2.1	110.00 ± 2.5	30.00 ± 2.1
3	Ajwa date's extract (T_2)	83.20 ± 3.4	129.00 ± 2.7	24.00 ± 2.0
4	Diazepam (S)	90.60 ± 2.5	136.80 ± 4.6	15.60 ± 3.6

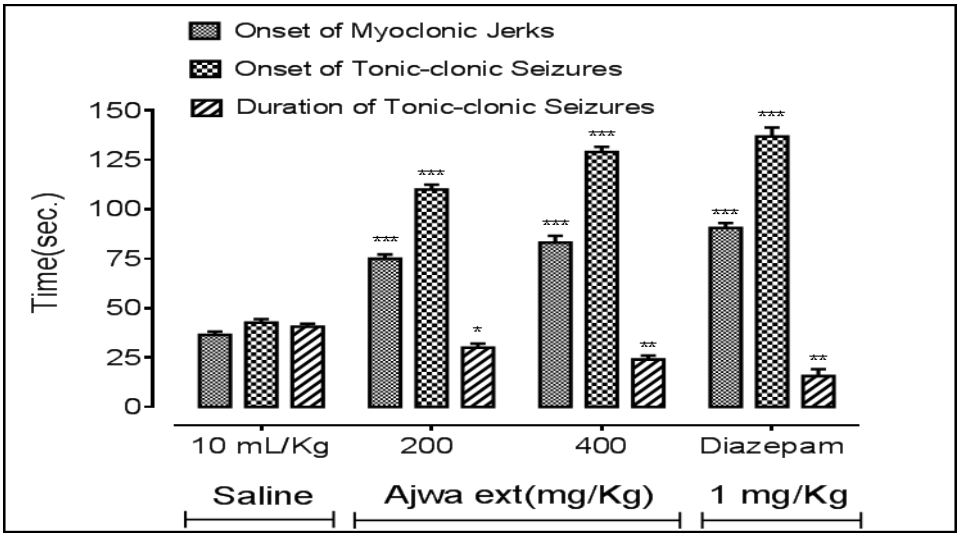

Figure 1: Time of onset of the myoclonic, tonic-clonic seizure and Duration of clonic phase of seizure (seizure latency) by control group, standard group and two test groups (Ajwa date's extract at two doses)

DISCUSSION:

Seizures were seen in all the groups. There was no statistically significant difference between the mean duration of clonic phase of the seizure, onset of myoclonic and tonic-clonic seizure of normal saline control group (36.45 ± 1.7, 42.67 ± 1.8, 40.60 ± 1.5). Diazepam (standard drug) prolonged the onset of myoclonic and tonic-clonic seizure (90.60 ± 2.5, 136.80 ± 4.6 sec respectively) in a statistically significant manner and this standard drug also shorten the duration of tonic-clonic seizure (15.60 ± 3.6) (Table 1, Figure 1). Test groups (T_1, T_2) prolonged the time of onset of seizure and decreased the duration of seizure, when compared to control (saline) group and these test groups showed the same effect when compared to standard drug (Diazepam) (Table 1, Figure 1). Ajwa date's extract at the dose of 200 mg/kg (Test group T_1) prolonged the onset of myoclonic and tonic-clonic seizure (75.00 ± 2.1, 110.00 ± 2.5 respectively) in a significant manner and decreased the duration of seizure (30.00 ± 2.1) compared to control (saline) group (Table 1, Figure 1).

Ajwa date's extract at the dose of 400 mg/kg (Test group T_2) also delayed the onset of myoclonic and tonic-clonic seizure (83.20 ± 3.4, 129.00 ± 2.7 respectively) in a significant manner and reduced the duration of seizure (24.00 ± 2.0) compared to control (saline) group (Table 1, Figure 1). When the two doses of Ajwa date's extract was compared among themselves, the test group T_2 showed better effect than test group T_1. It was observed that prolongation of the onset of myoclonic and tonic-clonic seizure and reduction of the duration of seizure by Ajwa date's extract at the dose of 400 mg/kg was greater than the dose of 200 mg/kg.

CONCLUSION:

Hydro-alcoholic extract of Ajwa date has *in vivo* anticonvulsant activity in the PTZ induced seizures and its anticonvulsant activity is comparable with the Diazepam. More studies are needed to investigate its exact mechanism and to evaluate the efficacy of hydro-alcoholic extract of Ajwa date in other seizures. Clinical trials to be conducted in human beings to evaluate its anticonvulsant activity.

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