

Research Article**Evaluation of anticonvulsant activity of Majoon Najah in experimental animal model**Zeba Afrin¹, Aisha Siddiqui^{2*}, M. A. Jafri³, Divya Vohora⁴, M. Asif²¹Research Associate, Central Council for Research in Unani Medicine Headquarters, Janakpuri, New Delhi, India²Assistant Professor, Department of Ilmul Advia, School of Unani Medical Education & Research, Jamia Hamdard, New Delhi, India³Professor, Department of Ilmul Advia, School of Unani Medical Education & Research, Jamia Hamdard, New Delhi, India⁴Professor and Head, Department of Pharmacology, School of Pharmaceutical Education and Research, Jamia Hamdard, New Delhi

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Abstract

Objective: To compare the anticonvulsant activity of Majoon Najah, its hydroalcoholic extract and granular form through Increased Current Electroshock Seizure (ICES) test in swiss albino mice. **Methods:** Majoon Najah, its hydroalcoholic extract and granular form were tested for anticonvulsant activity using ICES animal model. To evaluate the effect of test drugs on motor co-ordination, muscle co-ordination test by rotarod was carried out. **Results:** In ICES test Seizure Threshold Current (STC), duration of hindlimb extension (HLE) and percent protection were observed. It was found that MN ($p < 0.01$), HEMN and GMN ($p < 0.001$) significantly increased the seizure threshold current when compared with control. Although HEMN increased the STC more significantly than MN and GMN but intra-comparison between MN, HEMN and GMN showed no statistical significant variation in the activity. **Conclusion:** It can be concluded from the experiment performed that Majoon Najah possess significant anticonvulsant activity.

Keywords: Majoon Najah, anticonvulsant, ICES

Introduction

Epilepsy is the world's most common serious disorder of the brain according to World Health Organization (Anonymous, 2005). Epilepsy is the second most common chronic neurological condition seen by neurologists. It is approximated that there are 55,00,000 persons with epilepsy in India, 20,00,000 in USA and 3,00,000 in UK (Sridharan, 2002). It is estimated that around 50 million people in the world have epilepsy and 5% of the general population approximately experience at least one seizure at some time in their lives excluding febrile seizures. Epilepsy (*Sara*) is the cessation of all sensory faculties of a person and the person suddenly falls on the ground with involuntary movement (*Tashannuj*) of face and both upper and lower limbs accompanied with a frothy salivary discharge from mouth (Azam, 2010).

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Currently available antiepileptic drugs are synthetic compounds and have limited efficacy and their major side effects limit their use and cause difficulties in patient management. These drugs have no effect on epileptogenesis, which is a process that converts the normal circuitry of the brain into a hyperexcitable state and provide only symptomatic relief as these drugs suppress seizures. Moreover due to adverse effects, withdrawal symptoms, interactions with other drugs and economic burden antiepileptic drugs (AEDs) could not be used for long term. For example the main limitation of Phenobarbital is its tendency to alter cognition, mood and behaviour. AEDs prescribed to pregnant women may cause fetal anomalies including cognitive impairment, neural tube defects, congenital heart defects. A serious barrier to successful treatment in patients with epilepsy is noncompliance. The major reasons are inconvenient doses, complicated regimens and side effects. Despite massive funding for new AED development, the drugs lack safety and efficacy and about 30% of patients are still pharmaco-resistant (Wahab, 2010).

According to a survey WHO appraises that 80% of the world

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population reckon on medicines of plant origin for their primary healthcare (Kamboj, 2000). It has been approximated that in developed countries such as United States, plant drugs constitute 25% of the total drugs, whereas the contribution is as much as 80% in fast developing countries such as China and India. Hence, the economic importance of medicinal plants is much more to countries such as India than to rest of the world. The herbal products today signify safety in contrast to the synthetics that are regarded as unsafe to human and environment. Antiepileptic drugs with a better efficacy and safety are rarely available which reveal an immense need for developing newer effective and safe alternative antiepileptic compounds. Development of herbal anticonvulsant drugs as an alternative to synthetic drugs will be a precious contribution to health care system. In recent years, some of the herbal drugs have already been investigated for their anticonvulsant activity which have demonstrated promising results (Malvi *et al.*, 2011). Extensive literature survey reveals that Majoon Najah is an age old, time tested polyherbal preparation of Unani system of medicine which is commonly used for the treatment of epilepsy (*Sara*) and other neurological disorders. In classical Unani literature it has been described to be useful in *Sara* (Epilepsy) (Hassan, YNM), *Malikholia* (Melancholia) (Anonymous, 2006; Anonymous, 1986), *Ikhtenagurrahama* (Hysteria) (Anonymous, 2006), Insanity (Anonymous, 1986) etc; but no scientific study has been conducted in this aspect of Majoon Najah to validate its antiepileptic activity. In present context there is a need to evaluate this formulation on scientific parameters to validate its efficacy, so that it can be utilized in future for the treatment of convulsive disorders. Hence, it was selected for the present study to evaluate its anticonvulsant activity.

Material and methods

All the test formulations (Majoon Najah, Granules and hydroalcoholic extract of ingredients of Majoon Najah) were

prepared in the Dept. Of Ilmul Advia, School of Unani Medicine, Jamia Hamdard. Before starting the animal experiment, the research protocol was submitted to the IAEC, Jamia Hamdard, New Delhi for ethical approval. The protocol was approved vide Reg. No. 173/GO/Re/S/2000/CPCSEA.

Procurement and authentication of raw drugs

All the required ingredients of Majoon Najah were procured from the raw drug dealers in Khari Baoli market, Old Delhi under the supervision of Guide. All the raw drugs were identified and authenticated by the expert from Dept. of Botany, School of Chemical & Life Sciences, Jamia Hamdard, New Delhi.

Preparation of Majoon Najah

Majoon Najah was prepared as per the procedure mentioned in the pharmacopeia 'National Formulary of Unani Medicine (NFUM) Part II, Vol. I. The ingredients of Majoon Najah are given in table 1.

MN is prepared as per the procedures, mentioned in the pharmacopeia Part II, Vol. I of National Formulary of Unani Medicine (NFUM).

Powdering the ingredients

As per the classical method, *Halailajat* 'Three Myrobalan fruits' (from S. No. 1 to 4) are first dried to evaporate their moisture content and pounded in an iron mortar. Initially gentle pounding is employed to break the drugs into small pieces then vigorous pounding is done till they are ground into coarse powder. The powder is then passed through appropriate mesh sieve (Chaudhary, 2013). The remaining ingredients (from S.No.5 to 8) are dried, powdered and sieved separately.

Rubbing (*Tad'heen or Charb*) the *Tirphala* with almond oil or sesame oil or Ghee:

Table 1. Ingredients of Majoon Najah

S. No.	Unani Name	Botanical Name	Parts Used	Quantity
1.	Post-e-halelakabli	<i>Terminalia chebula</i> Retz	Fruit	40g
2.	Post-e-Balela	<i>Terminalia bellerica</i> Roxb	Fruit	40g
3.	Aamla	<i>Emblica officinalis</i> Gaertn.	Fruit	40g
4.	Halela Siyah	<i>Terminalia chebula</i> Retz	Fruit	40g
5.	Turbud	<i>Operculinaturpethum</i> Linn	Root	40g
6.	Bisfayej	<i>Polypodium vulgare</i> Linn	Root	20g
7.	Aftimoon	<i>Cuscuta reflexa</i> Roxb.	Whole plant	20g
8.	Ustukhuddus	<i>Lavandula stoechas</i> Mill.	Flowers	20g
9.	Qandsafaid (Sugar)			750g

Table 2. Experimental design

S. No.	Groups	Agents	Route	Dosage	Duration
I	Control	Distilled water	Oral	10ml/kg	7days
II	Standard	Phenytoin	Oral	15mg/kg	7days
III	Test Group A	MN	Oral	1700mg/kg	7days
IV	Test Group B	HEMN	Oral	260mg/kg	7days
V	Test Group C	GMN	Oral	600mg/kg	7days

MN= MajoonNajah, HEMN=Hydroalcoholic Extract, GMN=Granules of MajoonNajah

Table 3. Experimental design

S. No.	Groups	Agent	Route	Dosage	Duration
I	Test Group A	MN	Orally	1700mg/kg	7days
II	Test Group B	HAE	Orally	260mg/kg	7days
III	Test Group C	GMN	Orally	600mg/kg	7days

MN= MajoonNajah, HAE= Hydroalcoholic Extract, GMN= Granules of Majoon Najah

Tad'heen or Charb is the process of correction or detoxification in which dry drug is made oily or rubbed with some special oil. This terminology of pharmaceuticals is often used for *Tirphala*. The powdered *Tirphala* (Separately or with other ingredients of *Majoon* are rubbed with one of the following oils:

Raughan Badam (Almond oil) (Anonymous, 2007)

Raughan Zard (Cow Ghee) (Anonymous, 2007; Antaki, 1899)

Raughan Bed Injeer (Castor oil) (Choghtai, YNM)

Mixing the rubbed powder in the *Qiwam*:

For making *Majoon* or any of its allied preparations, *Qiwam* (Base) of different consistencies is generally made, depending on the nature of ingredient drugs to be used in a particular formula. The ingredient drugs in a *Qiwam* may be used either in powder or liquid form.

The *Qiwam* is generally made by adding *Aab* (water), *Arq* (Distillate) or *Aab e Samar* (Fruit Juice) etc., in any of the bases of purified Honey with Sugar, Candy or Jaggery etc., and boiled over a low fire till it acquires a required consistency. The bases are generally purified by adding *Aab e Leemu* (Lemon juice), *Satt e Leemu* (Lemon extract) or *Shibb e Yamani* (Alum) etc. Afterwards, the ingredient drugs are mixed in it, to prepare *Jawarish*, *Majoon*, *Itrifal*, *Halwa*. For making *Majoon* or any of its preparations the consistency of *Qiwam* of *Majoon* is three *Tar* (consistency) (Anonymous, 2007).

Total 250g of powder was prepared from ingredients of MN and weight of sugar was three times of total weight of ingredients i.e. 750g. Sugar (750g) was taken in a container and 225ml of water was added to it. Then 2-3g of benzoic acid and citric acid was

added to it as a preservative. Then it was heated on heating mantle on low flame with continuous stirring until boiling was started. Just after the initiation of boiling, container was removed from the flame and then all the powdered ingredients were added and mixed in the prepared *Qiwam* to prepare MN. Then it was stored in an airtight chamber.

Preparation of Hydroalcoholic extract of MN (HEMN)

All the crude ingredients of MN were kept in a drying oven at 40°C for about 30min to evaporate moisture and powdered in an electrical grinder. The powder obtained was rubbed with *Raughan-e-Badam* and then extracted in soxhlet's extractor with hydroalcoholic solvent (ethanol and distilled water in ratio 80:20) for about 6 hours at the fixed temperature of 80°C. The liquid extract cooled and filtered by Whatmann filter paper No.40. Then the filtrate was concentrated over steam bath till it dried completely. The resultant residue was collected and stored for further use.

Preparation of sugar free granules (GMN) (Gennaro, YNM)

Granules were prepared using wet granulation technique. The powdered ingredients were size reduced and passed through mesh sieve No.80. Then, all the powdered drugs were rubbed (*charb*) with *Raughan-e-Badam*. After that, binders like sodium Carboxymethyl Cellulose (Na-CMC) and Hydroxypropyl Methyl Cellulose (HPMC) were mixed with powder using a little amount of distilled water and a doughy mass was formed. The dough was passed through sieve No. 10 and superimposed on sieve No. 44, were dried in an oven and taken as the selected formulation and for further experiment.

Comparative study for anticonvulsant activity

To compare the activity of MN, HEMN and GMN, anticonvulsant activity was evaluated in mice through Increased Current Electroshock Seizures (ICES) test and Muscle Inco-ordination test by Rotarod.

Experimental animals

The study was carried out in Swiss albino mice of either sex weighing 20-25 gm, 2-3 months old. The animals were procured from Central Animal House Facility, Jamia Hamdard, New Delhi.

The animals were given a period of one week prior to the experiment to adjust the standard laboratory conditions. They were maintained under standard laboratory conditions all through the experimental period and were provided with standard rodent diet and water *ad libitum*. They were housed in clean polypropylene cages at room temperature/ humidity $25\pm 2^{\circ}\text{C}/45\text{-}55\%$. The animal care procedures and experimental protocol were in according to the guidelines of CPCSEA. The overnight fasted (water *ad libitum*) animals were transferred to the laboratory one hour prior to the beginning of the experiment.

Dosage of test drugs

The dose of test drugs for mice was calculated by multiplying the human dose with conversion factor of 12 by method of Freireich et al. The human therapeutic dose of MN is 5-10g (Anonymous, 2005; Anonymous, 2006) as mentioned in the classical Unani literature. The higher dose of MN was given to the mice in present study. The dose of MN for Swiss albino mice was calculated by factor twelve and found to be 1700mg/kg. Since the hydroalcoholic extract of the test drug was used so the dose of extract was calculated on the yield percentage of extract with reference to the dose of crude drug which was found to be 44.22%. So the dose of extract was found to be 265 mg/kg which was rounded off as 260mg/kg. The dose of sugar free granules of MN was calculated as 600mg/kg by subtracting the weight of sugar from original formula.

Distilled water and phenytoin (standard drug) were given orally in the dose of 10ml/kg, 15mg/kg body weight respectively.

All the test drugs (MN, HEMN, GMN) and standard drug were diluted with distilled water to the desired concentration for dose administration to the mice. All the drugs were administered once orally via gauge needle in volume of 1.5-2ml.

Screening anticonvulsant activity

Comparative screening of test drugs (MN, HEMN, GMN) for anticonvulsant activity was done using Increased Current Electroshock Seizures (ICES) test as proposed by Kitano et al, 1996 and Muscle Inco-ordination Test by Rotarod.

Increased Current Electroshock Seizures (ICES) Test

This test was carried out by the method described by Kitano et al. (1996). Male swiss albino mice were taken. The mice were divided into five groups of 6 mice each. The mice of first group were given distilled water in the dose 10ml/kg (control group) for 7 consecutive days; Group II were given Phenytoin (standard drug) in a dose of 15mg/kg orally, while Group III, IV and V were given test drugs i.e. 1700mg/kg of MN, 260mg/kg of hydroalcoholic extract and 600mg/kg of prepared granules orally respectively. Test drugs and standard drug were administered for 7 consecutive days orally.

On 7th day, 1h later after administration of test and standard drug, they all were treated with electric shock to induce convulsions. The seizure threshold was measured for each individual animal for studying the anticonvulsant effect of drugs. Briefly, in the modified method, starting with a current of 2mA, electroshock was determined via ear electrodes, as a single train of pulses (square wave, 0.2s duration) of linearly increasing current intensity of 2mA/2s, until tonic hind limb extension (HLE) occurred or 30mA current (STC) for that animal. If HLE was not observed even with 30mA current, electroshock was discontinued and this current was recorded as the Seizure Threshold Current (STC). Duration of hindlimb extension was also noted (Kitano et al., 1996).

Muscle Co-ordination test by Rotarod

Male swiss albino mice were taken. The mice were divided into three groups of 6 mice each. The mice of group I, II and III were given test drugs i.e. 1700mg/kg of MN, 260mg/kg of hydroalcoholic extract and 600mg/kg of prepared granules orally for 7 consecutive days.

Preselected mice (animals that stayed for at least 3 min on the rotating bar, 24h before testing) were placed on the horizontal rotating bar (diameter 2.5cm, 16rpm) of the rotarod apparatus, 1h after the treatments on 7th day. Total time spent on the rotating bar during a 2min session was registered using a stopwatch and the number of fall during the session was also recorded (Radha & Goel, 2013).

Statistical analysis

All the values are expressed as Mean \pm SEM (Standard error of mean). The statistical significance was determined by One way ANOVA followed by Dunett's t Test. Values $p < 0.05$, $p < 0.01$ were considered as significant and $p < 0.001$ as highly significant.

Results and discussion

Comparative study of Majoon Najah, its hydroalcoholic extract and granules of ingredients of Majoon Najah for anticonvulsant activity

The test drugs (MN, HEMN and GMN) did not produced any inco-ordination as the animals overstayed on the revolving rod beyond 3min, much similar to the control animals.

Epilepsy is the second most common chronic neurological condition seen by neurologists (Sridharan, 2002). Currently available antiepileptic drugs are synthetic compounds and have limited efficacy and their major side effects limit their use and cause difficulties in patient management (Wahab, 2010). Antiepileptic drugs with a better efficacy and safety are rarely available which reveal an immense need for developing newer effective and safe alternative antiepileptic compounds.

Majoon Najah (MN) is one of the important Unani semisolid polyherbal formulations which is traditionally used for the treatment of various neurological disorders like epilepsy, hysteria, melancholia, insanity, schizophrenia etc. It is composed of 8 ingredients viz. Halailasiyah (*Terminalia chebula*), Halailakabli (*Terminalia chebula*), Balela

(*Terminalia bellirica*), Amla (*Emblica officinalis*), Turbud (*Operculina turpethum*), Aftimoon (*Cuscuta reflexa*), Bisfayej (*Polypodium vulgare*) and Ustkhudoos (*Lavandula stoechas*).

According to Unani concept, the causative matter responsible for epilepsy is mostly phlegmatic and sometimes black bile is responsible for it (Razi, 1997; Khan, 2010).

According to Unani literature, Halailasiyah and Halailakabli (*Terminalia chebula*) possess brain tonic activity and has purgative property for phlegm and black bile. Halaila also possess *Mufattehsudad* (deobstruent), *Mudir-e-baul* (diuretic) and *Muqawwi Meda* (stomachic) properties (Hakeem, 2002; Kabiruddin, 2000). Experimental studies revealed that it has significant anticonvulsant, neuroprotective, anxiolytic and antioxidant activities (Cheng, 2003; Senthil & Subramanian, 2007; Shekhar, 2013; Chang & Lin, 2012). The ethanolic extract of *Terminalia chebula* was evaluated for anticonvulsant

Table 4. Effect of MN, HEMN and GMN in ICES induced convulsions

S. No.	Groups	Dose (mg/kg, p.o.)	Seizure threshold current (mA)	% Protection from seizure	Duration of hind limb extension (sec) Mean±SEM
I	DW (Plain control)	10ml/kg	13.4±0.68	0	8.66±2.20
II	PHT (Standard control)	15mg/kg	28.80±0.37***	83.33	2.03±0.95**
III	MN (Test group A)	1700mg/kg	20.2±1.15**	50	4.20±0.73*
IV	HEMN (Test group B)	260mg/kg	25.6±1.12***	66.67	3.56±0.34*
V	GMN (Test group C)	600mg/kg	24.2±2.57***	66.67	4.01±0.46*

Each value is represented as Mean ±SEM, No. of animals (n)=6, DW=standard (PHT)=Phenytoin, MN= Majoon Najah, HEMN=Hydroalcoholic extract of ingredients of MajoonNajah, GMN=Granules of Majoon Najah. Treatment duration=7 days. One way ANOVA followed by Dunett's t Test. *p<0.05, **p<0.01, ***p<0.001 vsGroup I (Plain control)

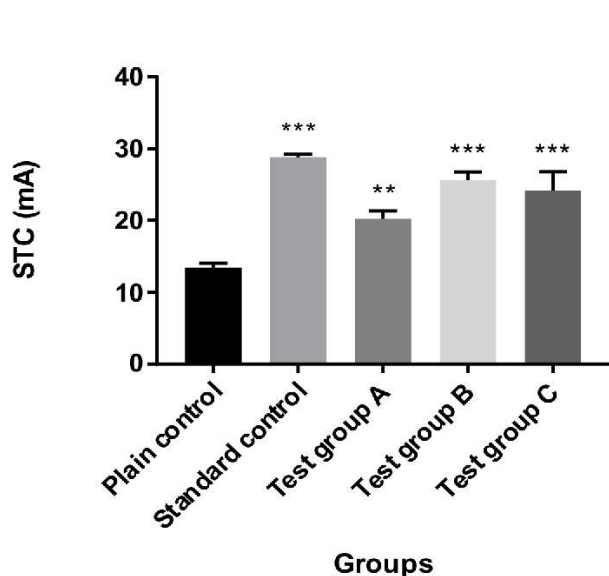


Figure 1. Effect of MN, HEMN and GMN on seizure threshold current (STC) during ICES test

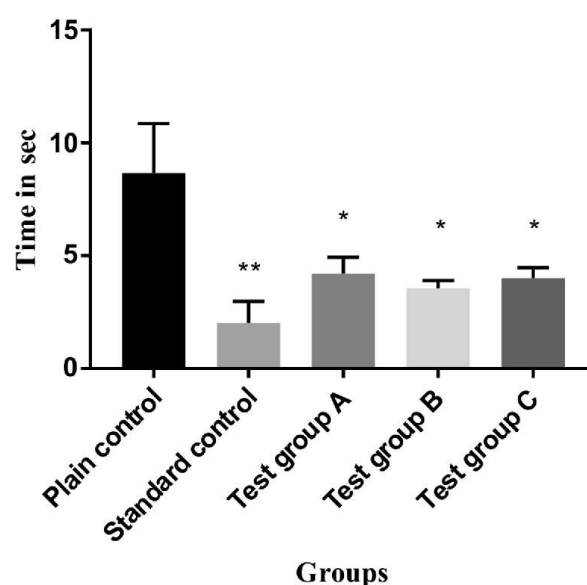


Figure 2. Effect of MN, HEMN and GMN on duration of HLE during ICES test

Table 5. Effect of MN, HEMN and GMN on duration of stay on revolving rod of rotarod apparatus

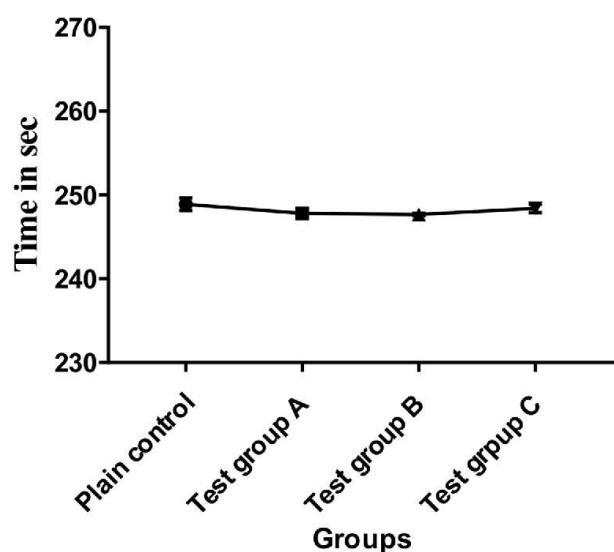
S. No.	Groups	Dose (mg/kg, p.o.)	Duration of stay on revolving rod (after training)
1	Distilled water (Plain control)	10ml/kg	248.9±0.75
2	MN (Test group A)	1700mg/kg	247.8±0.18
3	HEMN (Test group B)	260mg/kg	247.7±0.14
4	GMN (Test group C)	600mg/kg	248.4±0.48

Each value is represented as Mean \pm SEM, No. of animals (n)=6, DW=standard (PHT)=Phenytoin, MN= MajoonaNajah, HEMN=Hydroalcoholic extract of ingredients of MajoonaNajah, GMN=Granules of MajoonaNajah. Treatment duration=7 days. One way ANOVA followed by Dunnett's t Test. No statistical significant difference ($p>0.05$)- Test group A, B & C vs Group I (Plain control)

activity. It reduced the duration of seizures produced by maximal electroshock and delayed the latency of seizures produced by pentylenetetrazole and picrotoxin. The study demonstrated that ethanolic extract of *Terminalia chebula* has anticonvulsant activity (Debnath et al., 2010).

Balela (*Terminalia bellirica*) has Muqawwi-e-dimagh (brain tonic) and Mushil (purgative) properties (Kirtikar & Basu, 1975; Khare, 2007). Experimentally it has been reported to possess antioxidant and antianxiety properties (Hazra et al., 2010; Chandra et al., 2017). *T. Chebula*, *T. Bellirica* and *E. officinalis* were evaluated for in vitro antioxidant and reactive oxygen species scavenging activities and the study conclude that 70% methanol extracts of *T. chebula*, *T. bellirica* and *E. officinalis* imposes the fact that it might be useful as potent source of natural antioxidant.

Amla (*Emblica officinalis*) has Muqawwi-e-dimagh (brain tonic) activity and is Mushil-e-balghamwasauda (purgative for phlegm and black bile) (Hakeem, 2002; Anonymous, 2007). It has been reported experimentally to have anticonvulsant and

**Figure 3.** Effect of MN, HEMN and GMN on duration of stay on revolving rod during Rotarod test

antioxidant effects. *E. officinalis* was evaluated for anticonvulsant activity and it was concluded that hydroalcoholic extract of *E. officinalis* dose-dependently increased the latencies of myoclonic jerks and completely abolished generalized tonic seizures produced by PTZ (Golechha et al., 2010; S. Khopde et al., 2001).

Turbud (*Operculina turpethum*) has Muqawwi-e-asaab (nervine tonic), Mufattehsudad (deobstruent) and Mushil-e-balghamwasauda (purgative for phlegm and black bile) actions. Various studies suggest that it has antioxidant activity (Anbuselvam et al., 2007). *O. turpethum* showed the presence of glycosides, saponins, flavanoids, steroids and carbohydrates. Turpethin is mainly responsible for its purgative action.

Bisfaj (*Polypodiumvulgare*) has Dafesara (antiepileptic), Mushil-e-balghamwasauda (Purgative for phlegm and black bile) actions. It is reported experimentally to possess significant anticonvulsant activity (Dar et al., 2012).

Aftimoon (*Cuscutareflexa*) has Mufattehsudad (deobstruent) and Mushil-e-balghamwasauda (Purgative for phlegm and black bile) actions. Experimentally it is reported to have anticonvulsant anxiolytic and antioxidant effects (Yadav et al., 2000; Thomas et al., 2015).

Ustukhudoos (*Lavandulastoechas*) has Muqawwi-e-asaab (nervine tonic), Mufattehsudad (deobstruent), Muqawwi-e-dimagh (brain tonic) and Dafe Sara (anticonvulsant) actions. Various experimental studies suggest that it possess significant anticonvulsant and antioxidant activities. *L. stoechas* was evaluated for anticonvulsant activity and was concluded that it increased the latency and a reduction of level of the severity of convulsions. Complementary test suggested that this activity is related with the blocking of canals of calcium. The inhaling lavender oil vapor blocked pentylenetetrazole- and nicotine-induced convulsion and electroshock convulsion in mice (Sebai et al., 2013; Miraj, 2016). It may safely be concluded that MN possess anticonvulsant activity due to the above mentioned actions

of ingredients of test formulation (MN).

For comparative screening of anticonvulsant activity of classical MajoonNajah (MN), its prepared hydroalcoholic extract (HEMN) and granular form (GMN), one experimental models was selected i.e. Increased Current Electroshock Seizure (ICES) test for swiss albino mice. ICES test is a model of generalized tonic-clonic type seizure and is useful for evaluation of both the anti- and pro-convulsant activities of drugs (Kitano et al, 1996).

In ICES test Seizure Threshold Current (STC), duration of hindlimb extension (HLE) and percent protection were observed. It was found that MN ($p < 0.01$), HEMN and GMN ($p < 0.001$) significantly increased the seizure threshold current when compared with control. Although HEMN increased the STC more significantly than MN and GMN but intra-comparison between MN, HEMN and GMN showed no statistical significant variation in the activity. MN, HEMN, GMN significantly ($p < 0.05$) decreased the duration of hindlimb extension when compared with control although it was less significant than standard drug ($p < 0.01$). In control group all the animals died whereas 83.33% protection was observed in the animals of standard group. In MN treated group there was 50% protection from death and 66.67% protection was found in both HEMN and GMN treated group.

The convulsion in ICES is due to the disturbed activity of GABA in the brain and electroshock causes the inhibition of GABA release and this in turn may inhibit GABA synthesis (Sermeta et al., 1998). The mechanism of convulsion in ICES test is unclear although it may be due to the release of various neurotransmitters. It is probable that the MN, HEMN and GMN (test drugs) may have some connection in the cascade of events in neurohumoral transmission.

Several studies have indicated that plants containing flavonoids and saponins have significant anticonvulsant activity (Jager & Saaby, 2011). The phytochemical tests revealed the presence of alkaloids, flavanoids, phenols, saponins in the extract of MN. It seems that alkaloids, flavanoids and phenols present in the extract might be responsible for the observed anticonvulsant activity. Anticonvulsant activity of the MN may also be attributed to the cumulative anticonvulsant effect of all of the ingredients of MN.

It is reported that most of the antiepileptic drugs cause ataxia and adverse effects on cognition and behaviour. So it is important to screen the effect of any anticonvulsant drug on muscle co-ordination. To evaluate the effect of drug on motor co-ordination, muscle co-ordination test by rotarod was carried out. In muscle co-ordination test by rotarod, time spent on revolving rod of rotarod apparatus was observed. Mice of treated groups (MN, HEMN & GMN) overstayed on the revolving rod beyond 3min much similar to the mice of control group. There was no

statistical significant difference ($p > 0.05$) between mice of treated group and control group. The findings of this test suggest that the test drugs (MN, HEMN and GMN) did not produced any motor inco-ordination. So, MN, HEMN and GMN are safer than conventional antiepileptic drugs.

It can be concluded that the administration of MN, HEMN & GMN show promising anticonvulsant activity in ICES test and intra-comparison of these test drugs (MN, HEMN & GMN) did not produced any statistical significant difference ($p > 0.05$) in activity. So the study confirms that the hydroalcoholic extract of ingredients of MajoonNajah and its sugar free granules have anticonvulsant activity like the conventional form of MajoonNajah and there is no statistical significant difference in its effect.

The conventional form Majoon Najah, its hydroalcoholic extract and sugar free granules, all these forms did not produce any motor inco-ordination as none of the animals treated with test drugs fell off before 3min. Further studies are needed to evaluate exact chemical ingredient and mechanism of action of potential anticonvulsant effect of MajoonNajah.

Conflicts of interest

Not declared.

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