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Original Research Article

Preclinical evaluation of methanolic extract of *Malus domestica* peel on epilepsy in Swiss Albino mice using maximal electroshock test

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ABSTRACT

Background: Animal models for epilepsy have been used extensively to study the nature of seizures and epilepsy and to develop new therapies for epilepsy. In the present study, an effort has been made to evaluate the anticonvulsant activity of methanolic extract of *Malus domestica* peel (MEMDP) on epilepsy using maximal electroshock (MES) test in Swiss Albino mice.
Methods: The current study was prospective and single-center. Standard drugs: Phenytoin sodium 50 mg/kg orally (for MES test). Model used: MES. All drugs were administered orally to all 5 groups 45 minutes prior to experimentation with MES. Swiss Albino mice were weighed and marked, and then they were split into five groups of six at random (3 males and 3 females were included in each group).
Results: The MES test was performed on Swiss albino mice after grouping the animals. Six animals per group were used. Normal saline was used as a neutral control, and phenytoin sodium was used as positive controls. Doses of MEMDP used were 200 mg/kg, 400 mg/kg, and 800 mg/kg. MEMDP showed anticonvulsant activity with maximum activity at 400 mg/kg and 800 mg/kg body weight. The anticonvulsant activity of acute administration of 400 mg/kg and 800 mg/kg doses of MEMDP was comparable with phenytoin sodium at 50 mg/kg body weight (in the MES test).
Conclusions: The result of the present study indicates that MEMDP upon acute administration has significant anticonvulsant-like activity, which is comparable to phenytoin sodium.

Keywords: *Malus domestica,* Anticonvulsant activity, MES experimental model, Swiss Albino mice, MEMDP, Phenytoin sodium

INTRODUCTION

Epilepsy is coined from the Greek word “epilembanein” which means "to seize”.[1] Epilepsy is defined as a “disorder of brain function characterized by the periodic and unpredictable occurrence of seizures”.[2] It is the second most prevalent severe and long-lasting neurological disorder in the world.[3] It contributes roughly 1% of the global illness burden and affects about 50 million people worldwide. One fifth of the world's epilepsy cases are thought to occur in India, where there are an estimated 6-10 million instances.[2,4]

About 80% of epileptics live in low- and middle-income nations, where antiepileptic medication supply is typically

limited.[5] The antiepileptic medications (AEDs) that are currently on the market are synthetic compounds, and their pharmacology is completely symptom-specific. There is currently no effective preventative measure or treatment for individuals with epileptic seizures.[6] It might be challenging to decide which AED is best for a patient. For years, only a few of AEDs were available.

Animal models of epilepsy have been widely utilized to investigate the nature of seizures and epilepsy as well as to create novel treatments for the condition.[7] Preclinical testing of animal models is necessary to determine the safety and effectiveness of new AEDs before they are administered to human subjects.[8] The possibility that an investigational AED would show effectiveness in human clinical trials is obviously higher for animal models that are more predictive of any particular seizure type or illness.[9] The MES seizure models represent one of the two animal seizure models most widely used in the search for new AEDs.[10] In the present study, an effort has been made to evaluate the anticonvulsant activity of methanolic extract of MEMDP on epilepsy using MES test in Swiss Albino mice.[11,12]

METHODS

This single-center prospective study was carried out in the pharmacology department of the A. J. Institute of Medical Sciences and Research Centre in Mangaluru, India. The study ran from July 2015 to June 2016.

Study was approved by institutional ethical committee.

Institutional animal ethics committee (IAEC). clearance number: IAEC/01/2014/CPCSEA Date of clearance: 05/11/2014

All animals for the purpose of experimentation were obtained from the Central Animal House, A. J Institute of Medical Sciences and Research Centre, Mangaluru bearing registration number 1075/ac/07/CPCSEA.

Species used was Albino Swiss mice gender-30 males and 30 females age: Around 3 months

Number of animals used were 30.

Six mice per cage were kept in hygienic polypropylene cages in a regulated setting (26-28 ^{0}C) with a 12-hour light and dark cycle. They have unrestricted access to commercial pelleted food and water.[1]

The experiments were conducted at the Research Laboratory located in the Department of Pharmacology, AJIMS and RC during the month of November and December 2015. The mice were allowed to acclimate to these conditions for a week. Every effort was made to minimize the number of animals used and the suffering they experienced. All of the animals underwent rehabilitation at the Central Animal House facility after their experiments.

Plant material

Dried peel of *Malus domestica* from which an methanolic extract was prepared.

Methanolic extract of MEMDP which was obtained from the Department of Pharmacognosy, Srinivas College of Pharmacy, Mangaluru.

Apple peel collection and authentication

The peel of fuji apple were collected and weighed and lyophilized at minus 40º C. Methanolic extract of *Malus domestica* was obtained using Soxhlet apparatus with 70% methanol as solvent.

Standard drugs

Phenytoin sodium 50 mg/kg orally (for MES test).[11,12]

Vehicle

Normal saline 10 ml/kg used in the study.

Models used

Models used were MES.[11,12]

Study design

For each test, animals were divided into 5 groups with 6 animals in each group. The groups are as follows- Group I served as control and received normal saline. Group II received standard drug that is (Phenytoin sodium 50 mg/kg in MES test), group III received MEMDP at a concentration of 200 mg/kg. Group IV received MEMDP at a concentration of 400 mg/kg. Group V received MEMDP at a concentration of 800 mg/kg.

All drugs were administered orally to all 5 groups, 45 minutes prior to experimentation with MES. Swiss Albino mice were randomly assigned to five groups of six mice each after being weighed and marked. Each group consisted of three males and three females.

Normal saline (10 ml/kg) was administered orally to animals in Group I. Group II animals were given standard drug, phenytoin sodium 50 mg/kg (orally). Group III animals were given 200 mg/kg of MEMDP (orally). Group IV animals were given 400 mg/kg of MEMDP (orally). Group V animals were given 800 mg/kg of MEMDP (orally). 45 minutes after drug administration on day 1, the maximal electroshock was applied via trans auricular electrodes (moistened with saline solution before each application) separately to each mouse. The stimulus duration used was 0.2 sec and the electroshock was given

at the intensity of 12 mA, 50 hz. Latency, tonic flexion of the forelimbs, tonic extension of the hind limbs, and clonic convulsions were all detected in the animals. Recovery time was also recorded.[11,12] Drugs were administered at appropriate time to all 5 study groups from day 2 to day 14. On day 15, 45 minutes after drug administration maximal electroshock was again applied via trans auricular electrodes separately to each mouse of all 5 groups. The stimulus intensity and duration of electroshock remained same as that on day 1. Again, animals were observed for occurrence of latency, tonic flexion of fore limbs, tonic extension of hind limbs, clonic convulsions following stimulus.[11,12] Results of MES tests done on day 1 and day 15 were compared.

Table 1: Study groups in MES test.

Group	No. of animals	Drug	Dose/kg	Route
I	6	Normal saline	10 ml/kg	PO
II	6	Phenytoin sodium	50 mg/kg	PO
III	6	MEMDP	200 mg/kg	PO
IV	6	MEMDP	400 mg/kg	PO
V	6	MEMDP	800 mg/kg	PO

*MEMDP-Methanolic extract of *Malus domestica* peel, PO-per orally.

Mean values of all the parameters recorded in MES test models was calculated. Data is presented as Mean±SEM. The comparison between experimental and control group was performed using one-way ANOVA. Comparison between experimental and standard groups were done using Dunnett's t test. A p=0.05 or less was regarded as statistically significant. SPSS software (Statistical package for social services) Data analysis done using version 16.0.

RESULTS

In this experiment, the parameters for each animal were recorded in all 5 test groups (n=6). The parameters observed were: Latency, tonic flexion of forelimbs, tonic extension of hind limbs, clonic convulsions and recovery.

The study was carried out to assess the anticonvulsant activity of methanolic extract of MEMDP for screening antiepileptics. MES test was performed in Swiss albino mice after grouping the animals. Six animals per group were used. Normal saline was used as neutral control and phenytoin sodium and sodium valproate were used as positive control. Doses of MEMDP used were 200 mg/kg, 400 mg/kg, and 800 mg/kg. MEMDP showed anticonvulsant activity with maximum activity at 400 mg/kg and 800 mg/kg body weight.

The anticonvulsant activity of acute administration of 400 mg/kg and 800 mg/kg dose of MEMDP were comparable with phenytoin sodium at 50 mg/kg body weight (in the MES test).

Table 2: Anticonvulsant activity of MEMDP by MES induced seizures in Swiss Albino mice (day 1).

Groups	Latency (Sec)	Tonic flexion of fore limbs (Sec)	Tonic extension of hind limbs (Sec)	Clonic convulsions (Sec)	Recovery (Sec)
Control (Normal saline) 10 ml/kg	1.5±0.341	4.166±0.477	13.66±0.98	10.833±0.40	62.5±0.76
Phenytoin sodium 50 mg/kg	1±0.00 *	0±0.00**	0±0.0**	3.66±0.49**	0±0.0***
MEMDP 200 mg/kg	1.33±0.210*	3.166±0.70*	13.5±1.33*	13.5±1.33*	54.66± 3.45*
MEMDP 400 mg/kg	1.16±0.166*	1.166±0.74**	3.66±1.22**	4.66±0.494**	23.5±2.27**
MEMDP 800 mg/kg	1±0.00*	0±0.00**	1.016±1.04*	10.16±1.04*	24.833±1.95*

*N=6. The observation are mean±SEM. *p>0.05, **<0.05, *** p<0.01 as compared to control (ANOVA followed by Dunnett's multiple comparison test), MEMDP-Methanolic extract of *Malus domestica* peel.

Table 3: Anticonvulsant activity of MEMDP by MES induced seizures in Swiss Albino mice (day 15).

Groups	Latency (Sec)	Tonic flexion of fore limbs (Sec)	Tonic extension of hind limbs (Sec)	Clonic convulsions (Sec)	Recovery (Sec)
Control 10 ml/kg	1.33±0.210	3.833±0.60	13.66±0.88	13.33±12.02	63.33±0.88
Standard phenytoin sodium 50mg/kg	1.166±0.16*	0±0.00 ***	0±0.00***	3±0.44***	0±0.00 ***
MEMDP 200 mg/kg	1.666±0.16*	1.66±0.33 ***	3.5±0.428***	3±0.36 ***	10.33±0.66***
MEMDP 400 mg/kg	1±0.00*	0.833±0.54***	1.5±0.957***	1.833±0.654 ***	2.5±0.846***
MEMDP 800 mg/kg	1±0.00*	0±0.00***	1.833±1.16***	2.833±0.307 ***	4.66±0.666***

*N=6. The observation are mean±SEM. *p>0.05, **<0.05, *** p<0.01 as compared to control (ANOVA followed by Dunnett's multiple comparison test), MEMDP-Methanolic extract of *Malus domestica* peel.

DISCUSSION

The currently available drugs used for treating epilepsy are associated with many adverse effects. The development of inexpensive, safe, and effective anticonvulsant medicines derived from plants and other sources is therefore desperately needed. Plants and their phytoconstituents have an important role in the development of potent anticonvulsant agents.[13,14] Phytochemical screening provides basic information about the different classes of secondary metabolites present in a plant and fruit and the medicinal importance of such plant and fruit extracts.[15] It was earlier reported by Wolfe et al. that apple peel contains catechins, procyanidins, phloridzin, phloretin glycosides, caffeic acid, and chlorogenic acid, quercetin glycosides and catechins. The preliminary phytochemical screening of the ethanol extract of Malus domestics peel revealed the presence of flavonoids, polyphenols, chlorogenic acid, cyanidin-3-O-galactoside, rutin, quercetin glycosides and catechins.[16] Malus doemstica peel has a variety of health benefits such as improving skin tone, promoting hair growth, preventing and controlling respiratory diseases, controlling blood sugar, protecting from various cancers, as it is rich in fiber. Hence, it is considered a safe herbal medicine with very few and insignificant adverse effects.

The electroshock assay in mice is used primarily as an indication for compounds that are effective in grand mal epilepsy. Drugs are frequently screened for absence seizures or generalized tonic-clonic seizures using the MES-induced convulsion paradigm. MES causes several changes at the cellular level, disrupting the signal transduction in the neurons. MES causes cellular damage by facilitating the entry of Ca^{2+} into the cells in large amounts, prolonging the duration of convulsions.[17] Apart from Ca^{2+} ions, MES may also facilitate the entry of other positive ions like Na^{+}, blockade of which can prevent the MES-induced tonic extension.[18]

Currently available anticonvulsant drugs like sodium valproate and phenytoin sodium act by modulation of these ion channels.[19] On the other hand, drugs that antagonize NMDA receptors or potentiate opioids and GABA receptors are also reported to protect against MES-induced seizures.[20] Tonic hind limb extensions are evoked by electric stimuli which are suppressed by anti-epileptics.[21] MEMDP extract possesses anticonvulsant activity as evidenced by decreased duration of tonic hind limb extension in MES-induced convulsions. This study further confirmed the activity of currently available antiepileptic drugs that are clinically effective in the management of generalized tonic-clonic and partial seizures, such as carbamazepine, phenytoin and clonazepam. MEMDP suppressed hind limb tonic extension (HLTE) in MES. On day 1 and day 15 there was a significant ($p<0.001$) decrease in the duration of tonic hind limb extension at all three doses of extract (200, 400 and 800 mg/kg) in MES model with maximum protection observed at 400 mg/kg and 800 mg/kg dose, as compared to the control group. It also decreased the number of clonic convulsions. However, the standard drug phenytoin sodium (50 mg/kg orally) and methanolic extract 800 mg/kg provided 100% complete protection. The ability of the extract to inhibit the TEHL in the MES as compared to Phenytoin sodium in this model suggests anticonvulsant activity, which could be beneficial in the management of generalized tonic-clonic and partial seizures.

The methanolic extract of MEMDP significantly and dose-dependently reduced the duration of tonic hind limb extension in MES experimental model. In the present study, the doses of 400 mg/kg and 800 mg/kg afforded protection to all animals. *Malus domestica* contains large quantities of ursolic acid and related compounds.[21] Ursolic acid (sometimes referred to as urson, prunol, malol, or 3-beta-3-hydroxy-urs-12-ene-28-oic-acid), is a pentacyclic triterpenoid that has been extensively found in fruit peels, herbs, and spices like thyme and rosemary. It was first discovered in the epicuticular waxes of apples in 1920. Ursolic acid obtained from Salvia officinalis was reported to have anti- inflammatory, antioxidative, antiprotozoal, antimutagenic and anticancer properties.[21]

The anticonvulsant activity seen in the present study may be due to the presence of ursolic acid in the peel. This implies that MEMDP may be effective as an anticonvulsant medicinal plant and its anticonvulsant effect may be by involving Gabanergic inhibitory and glutaminergic excitatory mechanisms or inhibition of the voltage gated sodium channel.[22] Our results also suggest the MEMDP extracts may be effective against human generalized myoclonic seizures and also absence ones.[23]

Our findings suggest that eating apple peels can be good for your health. Although they are frequently thrown away during the manufacturing of processed apple products, apple peels are evidently rich in bioactive and antioxidant components. Waste apple peels from apple sauce and canned apple manufacture should be regarded as a valuable product. The results obtained in this study have demonstrated that methanolic extract of MEMDP possesses anticonvulsant activity in animal models and this provides a rationale for its use in traditional medicine for the management of epilepsy. This study also reinforces the value of studying traditional resources (biologic and cultural) as sources of new drug leads. The limitations of the study were; it is an experimental study so it is difficult to extrapolate results of animal study directly on human. The present work did not include the identification of the active principal and its mechanism of action. Therefore, further research is required to elucidate specific mechanism(s) and active principles and the safety profile of the MEMDP as a medicinal remedy for convulsions.

CONCLUSION

Results of the study indicate that methanolic extract of *Malus domestica* has a definite anticonvulsant activity

effect. It significantly and dose-dependently reduced the duration of tonic hind limb extension in MES experimental model and also delayed the onset of clonic convulsions induced by pentylenetetrazole in Swiss Albino mice at 400 mg/kg and 800 mg/kg body weight comparable to standards, phenytoin sodium 50 mg/kg (in MES model).

In conclusion, the result of the present study indicates that MEMDP upon acute administration has significant anticonvulsant like activity which is comparable to phenytoin sodium.

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Ethical approval: The study was approved by the Institutional Ethics Committee IAEC/01/2014/CPCSEA

REFERENCES

1. Blume W, Luders H, Mizrahi E, Tassinari C, van Emde Boas W, Engel JJ. Glossary of descriptive terminology for ictal semiology: report of the ILAE task force on classification and terminology. Epilepsia. 2001;42(9):1212-8.
2. Rosa-Falero C, Torres-Rodríguez S, Jordán C, Licier R, Santiago Y, Toledo Z, et al. *Citrus aurantium* increases seizure latency to PTZ induced seizures in zebrafish thru NMDA and mGluR's I and II. Front Pharmacol. 2015;5:284
3. Sridharan R. Epidemiology of epilepsy. Curr Sci. 2002;82(6):664-70.
4. Reynolds E. Epilepsy in the world. Launch of the second Phase of the ILAE/IBE/WHO Global Campaign against Epilepsy. Epilepsia. 2001;43(6):46.
5. Birbeck G. Revising and refining the epilepsy classification system: Priorities from a developing world perspective. Epilepsia. 2012;53(2):18-21.
6. Hema B, Bhupendra S, Saleem TS, Gauthaman K. Anticonvulsant effect of *Drosera burmanni* Vahl Int J Appl Res Nat. 2009;2(3):1-4.
7. Fisher RS. Animal models of the epilepsies. Brain Res Brain Res Rev. 1989;14(3):245-78.
8. Löscher W, Schmidt D. New Horizons in the development of antiepileptic drugs: Innovative strategies. Epilepsy Res. 2006;69(3):183-272.
9. Smith M, Wilcox KS, White HS. Discovery of antiepileptic drugs. Neurotherapeutics. 2007;4(1):12-7.
10. Kandratavicius L, Balista PA, Lopes-Aguiar C, Ruggiero RN, Umeoka EH, Garcia-Cairasco N, et al. Animal models of epilepsy: use and limitations. Neuropsychiatr Dis Treat. 2014;10:1693-705.
11. Vogel HG, Hock FJ, Maas J, Mayer D. Drug discovery and evaluation, safety and pharmacokinetics assays. 3 edition. New York: Springer-Verlag. 2006.
12. Chandrashekar R, Adake P, Rao SN. Anticonvulsive activity of ethanolic extract of Acorus Calamus rhiozome in swiss albino mice. J Sci Inno Res. 2013;2(5):846-51.
13. Kumar KS, Kota K, Tahashildar J, Ragavendhra P. Antiepileptic activity of ethanolic extract of *Biophytum sensitivum* (L.) DC in Animal models. Int J Curr Res Aca Rev. 2015;3(7):23-30.
14. Wolfe K, Wu X, Liu RH. Antioxidant activity of apple peels. J Agri Food Chem. 2003;51(3):609-14.
15. Shabbir M, Khan MR, Saeed N. Assessment of phytochemicals, antioxidant, anti- lipid peroxidation and anti-hemolytic activity of extract and various fractions of *Maytenus royleanus* leaves. BMC Complement Altern Med. 2013;13:143.
16. Giomaro G, Karioti A, Bilia AR, Bucchini A, Giamperi L, Ricci D, et al. Polyphenols profile and antioxidant activity of skin and pulp of a rare apple from Marche region (Italy). Chem Cent J. 2014;8:45.
17. De Sarro G, Palma E, Costa N, Marra R, Gratteri S, De Sarro A, et al. Effects of compounds acting on GABA(B) receptors in the pentylenetetrazole kindling model of epilepsy in mice. Neuropharmacology. 2000;39(11):2147-61.
18. Nagakannan P, Shivasharan BD, Veerapur VP, Thippeswamy BS. Sedative and antiepileptic effects of *Anthocephalus cadamba* Roxb in mice and rats. Indian J Pharmacol. 2011;43(6):699-702.
19. Goldenberg MM. Overview of Drugs Used for Epilepsy and Seizures: Etiology, Diagnosis, and Treatment. Pharmacy Therap. 2010;35(7):392-415.
20. Inan SY, Buyukafsar K. Antiepileptic effects of two Rho kinase inhibitors, Y 27632 and fasudil, in mice. Br J Pharmacol. 2008;155(1):44-51.
21. Rodrigues MR, Kanazawa LK, das Neves TL, da Silva CF, Horst H, Pizzolatti MG, et al. Antinociceptive and anti-inflammatory potential of extract and isolated compounds from the leaves of Salvia officinalis in mice. J Ethnopharmacol. 2012;139(2):519-26.
22. Löscher W, Hönack D, Bloms-Funke P. The novel antiepileptic drug levetiracetam (ucb L059) induces alterations in GABA metabolism and turnover in discrete areas of rat brain and reduces neuronal activity in substantia nigra pars reticulata. Brain Res. 1996;735(2):208-16.
23. Gupta YK, Malhotra J, George B, Kulkarni SK. Methods and considerations for experimental evaluation of antiepileptic drugs. Indian J Physiol Pharmacol. 1999;43(1):25-43.

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