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ANTIDEPRESSANT ACTIVITY OF HYDRO-ALCOHOLIC EXTRACT OF FRUITS OF *MOMORDICA CYMBALARIA* HOOK. F IN ANIMAL MODELS

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ABSTRACT

The objective of the present study was to evaluate the antidepressant activity of hydro-alcoholic extract of fruits of *Momordica cymbalaria* Hook. F. Depression is the most common feature and it may range from a very mild condition to even severe depression which is called as psychotic depression. Furthermore, it is difficult to predict which patient will respond to any given treatment. In the traditional systems of medicine, many plants and formulations have been used to treat depression for thousands of years. In our present study we have selected behavioral despair models namely forced swimming and tail suspension tests. The main findings of present investigations suggest that the above extract posses antidepressant activity in mice forced swim test, tail suspension test and locomotor activity in rats. Hydro-alcoholic extract (HAEMC) was prepared from fruits of *Momordica cymbalaria* Hook. F. In the present study, the antidepressant effect of HAEMC-1(200mg/kg), HAEMC-2(400mg/kg) and HAEMC-3(600mg/kg) was examined using two behavioral models, the forced swim test (FST) and tail suspension test (TST) in mice. Duration of immobility was noted in both the models. Locomotor activity was also assessed in open field test. In our study, both imipramine and HAEMC significantly reduced the duration of immobility in both experimental models as compared to the animals in the control group. The antidepressant activity of HAEMC was comparable to that of standard drug imipramine. The results of the present study indicate the potential for use of HAEMC as an adjuvant in the treatment of depression.

KEY WORDS: Forced swim test, Tail suspension test, *Momordica cymbalaria* Hook. F, Depression, HAEMC.

1.INTRODUCTION

Depression is a common, debilitating, life-threatening illness with an increasing morbidity and mortality. According to the World Health report (WHO, 2001), approximately 450 million people suffer from a mental or behavioral disorder. This amounts to 12.3% of the global burden of disease, and will rise to 15% by 2020 (Reynolds, 2003). It is one of the most prevalent and costly psychiatric disorders worldwide, with 10-30% of women and 7-15% of men likely to suffer from depression in their life time (Malberg and Blendy, 2005).

In spite of the availability of antidepressant drugs like tricyclic antidepressants, selective reversible inhibitors of Monoamine Oxidase-A (MAO-A), selective serotonin reuptake inhibitors (SSRIs) and selective noradrenaline reuptake inhibitors (SNRIs), depression continue to be a major medical problem (Yu, 2002). Despite the development of new molecules for pharmacotherapy of depression, it is unfortunate that this disorder goes undiagnosed and untreated in many patients. Although the currently prescribed molecules provide some improvement in the clinical condition of patients, it is at a cost of having to bear the burden of their adverse effects (Hardman, 2001). Basic neuroscience offers the promise of improving our understanding of disease pathophysiology, identifying novel mechanisms that can be targeted by more effective pharmacotherapies and screening of herbal sources of drugs. These considerations implicate the search for new antidepressant agents that have a fast onset of action, with less side effects and a wider safety margin. Various plants are being used in complementary and alternative medicines for management of mood disorders.

Momordica cymabalaria Hook. F. (*M. cymbalaria)* belongs to the Cucurbitaceae family. The plant is a perennial herbaceous climber either allowed to trail on the ground or to climb on supports with the aid of tendrils. It is found in the South Indian states of Andhra Pradesh, Karnataka, Madhya Pradesh, Maharastra and Tamil Nadu as a weed. The plant is allowed to grow along bunds (boundary of fields), fences and even in the fields for the sake of fruits. However no regular cultivation is practiced. The flowering period is during November-December (Parvathi and Kumar, 2002). In Indian System of Medicine, The tuberous roots are reported to be abortifacient; the tuberous roots of male plant is used in ulcers, especially those caused by snake bites. The fruit is katu (pungent/bitter), tikta (bitter), deepanada (enriching digestive faculty), ruchikara (inducing taste), rakta and anila doshakara (causer of blood and nervous disorders). Tubers relieve arsha (piles), malarodha (constipation), visha (toxicity/effect of poisoning) and yoni nirgata dosha (internal urogenital disorders in women) and induce garbhasrava (abortion) and for open boils. The juice of leaves is used for whooping cough (Togunashi, 1977).

The different parts of the plant reported as cardio protective, anti-ovulatory, abortifacient, antimicrobial, anti-atherosclerotic, antidiabetic, antihyperlipedimic, anti-diarrheal activities (Vrusahbendra Swamy and Jayaveera, 2007; Vrusahbendra Swamy and Jayaveera, 2007; Raju, 2008; Vrusahbendra Swamy, 2008). The fruit of *Momordica cymbalaria* Hook. F contains flavonoids, tannins, alkaloids, carbohydrates, glycosides, Vitamin C, β-carotene,

polyphenols and amino acids (Momordicin, Ascorbigen, Pipecolic acid and unripe fruits contain Luteolin) etc (Parvathi and Kumar, 2002). By the light of above information the fruits of *Momordica cymbalaria* Hook. F was selected for evaluating its antidepressant activity due to its traditional use in the management of anxiety, stress, insomnia and hysteria.

2.MATERIALS AND METHODS

Animals: Adult Swiss Albino mice of either sex weighing 25-35 gm and albino Wistar rats of either sex weighing 150-200 gm from our breeding stock were used in this study. The animals were housed at 24±2^{o}C with 12:12 hrs light and dark cycle. They had free access to food and water *ad libitum*. The animals were acclimatized for a period of 7 days before the study. The study was conducted according to the Indian National Science Academy Guidelines for the use and care of experimental animals. The experimental protocol was approved by the Institutional Animal Ethics Committee (IAEC) of Gautham College of Pharmacy, Bangalore, Karnataka, India. Registration No. 491/01/c/CPCSEA.

Plant Material: *Momordica cymbalaria* Hook. F fruits were collected from the Bellary, Karnataka, India. The fruit was identified and authenticated by Regional Research Institute, Bangalore, Karnataka, India. (Voucher No: RRI/BNG/DSRU/F53/2006-07). The fruits were shade dried for 10 days and pulverized.

Preparation of Extract: The powdered plant material (500gms) was extracted with ethanol (70%v/v) by using soxhlet apparatus. The extract was concentrated under reduced pressure and stored in desiccator.

Experimental Design: (Dunham and Miya, 1957; Dhingra and Sharma, 2006)

Tail Suspension Test (TST): Tail suspension test commonly employed behavioral model for screening antidepressant like activity in mice, was first given by Steru *et al* (Steru *et al*., 1985). Animals were moved from their housing colony to laboratory in their own cages and allowed to adapt to the laboratory conditions for 1-2 hrs. Each mouse was individually suspended to the edge of a table, 50 cms above the floor, by adhesive tape placed approximately 1 cm from the tip of the tail. Each animal under test was both acoustically and visually isolated from other animals during the test. The total period of immobility was recorded manually for 6 min. animal was considered to be immobile when it didn't show any body movement, hung passively and completely motionless. The test was conducted in a dim lighted room and each mouse was used only once in the test. The observer, recording the immobility of animals, was blind to the drug treatments given to the animals under study. Group I (control group): normal saline (10 ml/kg p.o.). Group II: Imipramine (10 mg/ kg i.p.). Group III-V (HAEMC 200, 400 and 600 mg/kg p.o., respectively). After 60 min of drug administration the immobility time was recorded.

Forced Swim Test (FST): Forced swim test, the most frequently used behavioral model for screening antidepressant-like activity in rodents, was first proposed by Porsolt *et al* (Porsolt *et al*., 1977). The procedure was same as followed previously. Mice were individually forced to swim in open glass chamber (25 x 15 x 25 cms) containing fresh water to a height of 15 cms and maintained at 26±1^{o}C. At this height of water, animals were not able to support themselves by touching the bottom or the side walls of the chamber with their hind-paws or tail. Water in the chamber was changed after subjecting each animal to FST because "used water" has been shown to alter the behavior. Each animal showed vigorous movement during initial 2 min period of the test. The duration of immobility was manually recorded during the next 4 min of the total 6 min testing period. Mice were considered to be immobile when they ceased struggling and remained floating motionless in water, making only those movements necessary to keep their head above water. Following swimming session, mice were towel dried and returned to their housing conditions. Group I (control group): normal saline (10 ml/kg p.o.). Group II: Imipramine (10 mg/ kg i.p.). Group III-V (HAEMC 200, 400 and 600 mg/kg p.o., respectively). After 60 min of drug administration the immobility time was recorded.

Locomotor activity: (Poleszak et al., 2004): In general most of CNS acting drugs influence the locomotor activities in man and animals. In other word locomotor activity can be index of wakefulness (alertness) of mental activity (Kulkarni, 2005). Hence, locomotor acidity of animals treated with 200, 400 and 600 mg/kg of HAEMC was measured using actophotometer (IONCO, Ambala, India) to assess the possible effect on locomotor activity. Test animals were placed individually, in square arena of actophotometer for ten minutes and locomotor activity was recorded. The number of crossed light beams by the rat was recorded as the locomotor activity. Group I (control group): normal saline (10 ml/kg p.o.). Group II: Imipramine (10 mg/ kg i.p.). Group III-V (HAEMC 200, 400 and 600 mg/kg p.o., respectively). After 60 min of drug administration the immobility time was recorded.

Statistical Analysis: The mean ± S.E.M values were calculated for each group. The data were analyzed using one- way ANOVA followed by Dunnett's multiple comparison tests. $P< 0.05$ was considered to be statistically significant.

3.RESULTS

Tail Suspension Test (TST): The effect of HAEMC-1, HAEMC-2 and HAEMC-3 are shown in Table No 1 and Figure No 1. Duration of immobility is a measure of antidepressant activity was recorded in the last 4 minutes of 6 minutes test session. Statistically significant reduction in duration of immobility was observed in HAEMC-1, HAEMC-2 and HAEMC-3 treated animals. The effect of 600 mg/kg nearly equal to imipramine treated animals (P<0.001).

Forced Swim Test (FST): The effect of HAEMC-1, HAEMC-2 and HAEMC-3 are shown in Table No 2 and Figure No 2. Duration of immobility is a measure of antidepressant activity was recorded in the last 4 minutes of 6 minutes test session. Statistically significant reduction in duration of immobility was observed in HAEMC-1, HAEMC-2 and HAEMC-3 treated animals. The effect of 400 and 600 mg/kg dose of extract has nearly equal to imipramine treated animals (P<0.001).

Change in Locomotor Activity in Rats after treatment of HAEMC: Locomotor activity, quantify as locomotor score which was recorded after single dose administration, by placing the animal in the central area of actophotometer for 10 minutes test session. Locomotor activity of test animals receiving vehicle, imipramine, HAEMC-1, HAEMC-2 and HAEMC-3 were measured after 1 hr of oral administration. Although the increase in locomotor activity was observed with imipramine (10 mg/kg i.p) and HAEMC- 3 (600 mg/kg p.o) but effect on locomotor activity was not significant compared to vehicle treated animals. However, the change in locomotor activity after treatment of HAEMC (200 and 400 mg/kg) treated group not significant compared to vehicle treated animals. Locomotor activity after oral administration of HAEMC test formulation tabulated in table No 3 and effect on locomotion is shown in fig No 3.

DISCUSSION

The antidepressant effect of herbs has been paid more attention gradually because of increasing incidence of depression and predominance of traditional herbs in therapy. The effective components of herbs that have antidepressant-like effect include flavonoid, oligosaccharide, Polysaccharide, alkaloid and organic acid, etc (Barnes, 2001; Zhang, 2005; Guo, 2004). In the present study, hydro-alcoholic extract of fruits *Momordica cymbalaria* Hook. F (200, 400 and 600 mg/kg, p.o.) produced significant antidepressant-like effect in mice in both FST and TST. Both these models of depression are widely used to screen new antidepressant drugs (Porsolt, 1977; Jalfre, 1977). These tests are quite sensitive and relatively specific to all major classes of antidepressant drugs including tricyclics, serotonin-specific reuptake inhibitors, monoamine oxidase (MAO) inhibitors and atypical (Borsini and Meli, 1988).

In FST, mice are forced to swim in a restricted space from which they cannot escape, and are induced to a characteristic behavior of immobility. This behavior reflects a state of despair that can be reduced by several agents, which are therapeutically effective in human depression. The TST also induces a state of immobility in animals like that in FST. This immobility, referred as behavioral despair in animals, which is claimed to reproduce a condition similar to human depression (Willner, 1984). It has been argued that the TST is less stressful than FST and has greater pharmacological sensitivity (Thierry, 1986).

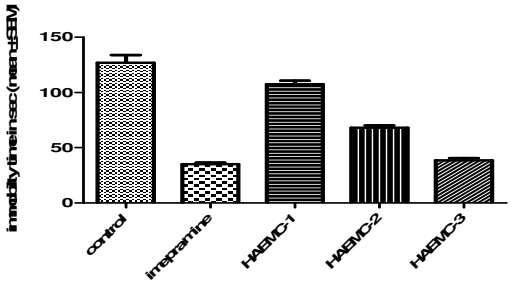
4.CONCLUSION

Thus, it may be concluded that *Momordica cymbalaria* Hook. F produced antidepressant-like effect in mice in both FST and TST. The efficacy of the *Momordica cymbalaria* Hook. F was comparable to that of imipramine. Further work was necessary to elucidate the mechanism of action involved in the antidepressant activity of *Momordica cymbalaria* Hook. F with special references to phytochemicals.

Table No-1. Effect of Hydro-alcoholic Extract of Fruits of *Momordica cymbalaria* Hook.F(HAEMC)TST

S.No.	Group	Treatment	Mean duration of immobility(sec)
1	Control	0.2ml/animal	127±6.928
2	Imipramine	10mg/Kg	35±1.732***
3	HAEMC-1	200mg/Kg	107.5±3.175**
4	HAEMC-2	400mg/Kg	68.0±2.309***
5	HAEMC-3	600mg/Kg	38.5±2.021***

Fig.No:1:Effect of HAEMC on duration of Immobility time in the TST



Values represents the mean ± SEM,*P< 0.05, ***P<0.001, when compared to vehicle treated animals.

Fig. No-2. Effect of HAEMC on duration of Immobility time in the FST

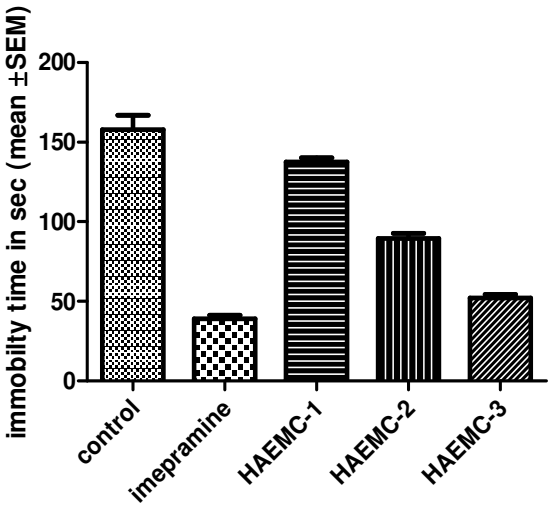


Fig. No-3. Change in Locomotor activity in Rats after treatment of HAEMC

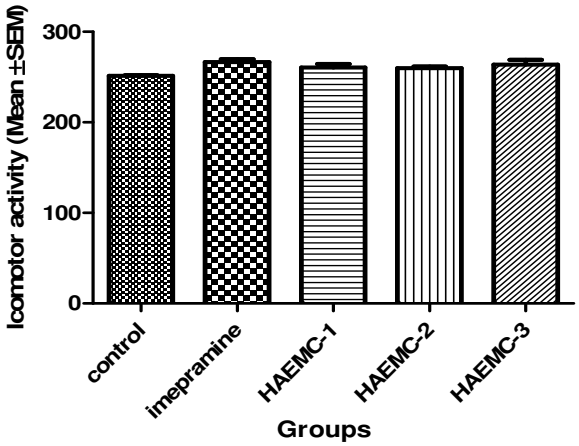


Table No-2. Effect of Hydro-alcoholic Extract of Fruits of *Momordica cymbalaria* Hook. F (HAEMC) FST

S.No.	Group	Treatment	Mean duration of immobility(sec)
1	Control	0.2ml/animal	157.8±9.114
2	Imipramine	10mg/Kg	39.0±2.309***
3	HAEMC-1	200mg/Kg	137±2.599*
4	HAEMC-2	400mg/Kg	89.50±3.175***
5	HAEMC-3	600mg/Kg	52.0±2.309***

Values represents the mean ± SEM,*P< 0.05, ** P<0.01, ***P<0.001, when compared to vehicle treated animals.

Table No-3. Effect of ethanol extract on locomotor activity in Rats (Actophotometer)

S.No.	Group	Treatment	Mean duration of immobility(sec)
1	Control	0.2ml/animal	251±1.155
2	Imipramine	10mg/Kg	266.5±3.175
3	HAEMC-1	200mg/Kg	260.5 ± 3.753^{ns}
4	HAEMC-2	400mg/Kg	259.5 ± 2.021^{ns}
5	HAEMC-3	600mg/Kg	263.5 ± 5.485^{ns}

Values represents the mean ± SEM (ns= Non significant, when compared to vehicle treated animals).

REFERENCES

Barnes J, Anderson L.A, Phillipson J.D, St John's wort (Hypericumperfortatum L.): a review of its chemistry, pharmacology and clinical properties, J.Pharm.Pharmac., 53, 2001, 583-600.

Borsini F, Meli A, Is the forced swimming test a suitable model for revealing antidepressant activity, Psychopharmacology, 94, 1988, 147-160.

Dhingra D, Sharma A, Anidepressant-like activity of *Glycyrrhiza glabra,* Neuropsychopharmacol.Biol. Psychiatry. 30, 2006, 449.

Dunham N.M, Miya T.S, A note on simple apparatus for detecting Neurological deficit in rats and mice, J.Am.Pharm., 46, 1957, 208-9.

Guo Y, Kong L, Wang Y, Huang Z, Antidepressant evaluation of polysaccharides from a Chinese herbal medicine Banxia-houpu decoction, Phytother.Res., 18, 2004, 204-207.

Hardman J.G, Limbird L.E, Goodman Gilman A, Goodman & Gilman's, The Pharmacological Basis of Therapueutics, 10th ed., The McGraw Hill Companies, New York, 2001, 451-469.

Jalfre M, Porsolt R.D, Bertin A, Behavioural despair in mice: a primary screening test for antidepressants, Arch.Int.Pharmacodyn.Ther., 229, 1977, 327-336.

Kulkarni S.K, Hand Book of Experimental Pharmacology, 3rd ed., Vallabh Publications, Delhi, 2005, 192.

Malberg J.E, Blendy J.A, Antidepressant action: To the nucleus and beyond, Trends.Pharmacol.Sci., 26, 2005, 631-8.

Parvathi S and Kumar V.J.F, Studies on chemical composition and utilization of the wild edible vegetable athalakkai (*Momordica tuberose),* Plant Foods for Human Nutrition, 57, 2002, 215–222.

Poleszak E, Szewczyk B, Kedzierska E, Wla P, Pilc A, Nowak G, Antidepressant and anxiolytic-like activity of magnesium in mice, Pharmacology Biochemistry and Behavior, 78, 2004, 7-12.

Porsolt R.D, LePichon M, Jalfre M, Depression: A new animal model sensitive to antidepressant treatment, Nature, 266, 1977, 730-732.

Raju K, Balaraman R, Hariprasad, Vinoth Kumar M, Ali A, Cardioprotective effect of *Momordica cymbalaria* Fenzl in rats with isoproteronal-indused myocardial injury, J.of clinical and diagnostic Research, 2, 2008, 699-705.

Reynolds E.H, Brain and mind: a challenge for WHO, Lancet, 361, 2003, 1924-1925.

Steru L, Chermat R, Thierry B, Simon P, The tail suspension test: A New method for screening antidepressant in mice, Psychopharmacology, 85, 1985, 367-370.

Thierry B, Steru L, Simon P, Porsolt R.D, The tail suspension test: ethical considerations, Psychopharmacol, 90, 1986, 284-5.

Togunashi V.S, Venkataram B.S, Yoganarasimhan S.N, Discussion on the orgin and identification of Kuduhunchi – A hitherto unknown Ayurvedic Drug, introduced by Rajanarahari, Journal of Research Indian Medicine Yoga and Homoeopathy, 12, 1977, 118-21.

Vrusahbendra Swamy B.M, Jayaveera K.N, Antimicrobial Properties of *Momordica cymbalaria* Hook. F, Pharmacologyonline, 3, 2007, 505-10.

Vrusahabendra Swamy B.M, Jayaveera K.N, Hepatoprotective and Antioxidant activities of *Momordica cymbalaria* Hook. F, Pharmacologyonline. 3, 2007, 491-504.

Vrushabebdra Swamy B.M, Jayaveera K.N, Ravindra Reddy K, Bharathi T, Anti-diarroeal activity of fruits extract of *Momordica cymbalaria* Hook. F, The Internet Journal of Nutrition and Wellness, 5, 2008, 2.

WHO, The World Health Report, Mental health: new understanding, new hope, Geneva, 2001, 16.

Willner P, The validity of animal models of depression, Psychopharmacol., 83, 1984, 1-16.

Yu Z.F, Kong L.D and Chen Y, Antidepressant activity of aqueous extract of *curcuma longa* in mice, Ethanopharmacol., 83, 2002, 161.

Zhang Y.Z, Li Y.F, Liu G, Yuan L, Huang S.J, Luo Z.P, Antidepressant effect of oligosaccharides extracted from *Morinda officinalis* on the learned helplessness rat model, Chin.J.Behavioral Med.Sci. (Chin)., 14, 2005, 309-311.