



ANTI-DEPRESSANT POTENTIAL OF GHIYA

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ABSTRACT

Lagenaria siceraria (Cucurbitaceae), popularly known as bottle gourd, lauki or ghiya, is a climbing plant, which bears hard-shelled and bottle-shaped gourds as fruits. Ghiya forms an excellent diet for people having digestive problems being rich in vitamins, iron and minerals. Since, it contains low calories, bottle gourd is an awesome foodstuff for shedding extra calories. The fruit possesses diuretic, emetic, and refrigerant properties. The ghiya (lauki) juice is helpful in constipation, premature graying hair, urinary disorders and insomnia. However, there are no reports in literature pertaining to CNS actions of *Lagenaria siceraria* fruit. In the light of above, the present study was undertaken to test the anti-depressant potential of *Lagenaria siceraria* juice (LSJ). *Lagenaria siceraria* juice was administered at various concentrations ranging from 4%-16% v/v orally to Swiss mice (30g), once daily for 15 successive days. The anti-depressant activity was measured using Forced Swim Test (FST) and Tail Suspension Test (TST). The efficacy of *Lagenaria siceraria* was compared to standard anti-depressant drugs viz: fluoxetine (20mg/kg, p.o), imipramine (15mg/kg, p.o) and phenelzine (20 mg/kg, p.o). *Lagenaria siceraria* significantly reduced the immobility time of mice in both FST and TST. Prazosin, Baclofen, Sulpiride and p-CPA significantly antagonized this reduction in immobility duration. Furthermore, *Lagenaria siceraria* juice inhibited the monoamine oxidase (MAO) enzyme and reduced significantly malondialdehyde (MDA) levels. These findings reveal the anti-depressant potential of ghiya.

KEY WORDS: *Lagenaria siceraria*, Anti-depressant, Forced swim test, Ghiya

INTRODUCTION

Mental depression is a chronic illness that affects a person's mood, thoughts, behavior and physical health. Depression is a complex disorder of unknown etiology, which is manifested by low mood, anhedonia, low energy levels, pessimism, guilty feeling and suicidal tendencies. It may range from a very mild condition, bordering on normality, to severe depression—sometimes called “psychotic depression” accompanied by hallucinations and delusions. Patients with major depression have symptoms that reflect changes in brain monoamine neurotransmitters, specifically norepinephrine, serotonin and dopamine¹. However, most of the marketed anti-depressant medicines exhibit serious side-effects. Therefore, the use of alternative medicines is increasing worldwide. Various herbal medicines (e.g. St. John's wort) have shown promising results in treating clinical depression and appear to be quite safe². *Lagenaria siceraria* (Cucurbitaceae) commonly known as bottle gourd/ghiya/lauki is reported to possess several medicinal properties such as, anti-oxidant activity³, anti-hyperlipidemic activity⁴, cardio protective activity⁵, analgesic activity⁶, anti-inflammatory activity⁷ and immunomodulatory activity⁸. Lauki contains several pharmacologically active photochemical such as amino acids, vitamins⁹, Fucosterol, campesterol¹⁰ and flavone-C glycosides¹¹. Furthermore, bottle gourd contains high amount of neurotransmitters such as serotonin, dopamine, adrenaline and noradrenaline¹². However, there is no scientific evidence for the therapeutic potential of ghiya (lauki) in neuropsychiatric disorders. Since serotonin and noradrenaline levels fall considerably in depression, we were interested to investigate the usefulness of ghiya (lauki) in depression.

MATERIALS AND METHODS

Objectives

The present study was undertaken to explore the anti-depressant potential of ghiya (*Lagenaria siceraria* juice) using forced swim test and tail suspension test. An attempt

has also been made to determine the underlying mechanism of action of ghiya (lauki) by co-administration of agents modulating noradrenaline, serotonin and malondialdehyde levels.



Ghiya (Lauki) Vegetable

Plant material

The fresh bottle gourd (*Lagenaria siceraria*) was purchased from local market of Hisar and got authenticated from Raw Materials Herbarium and Museum, National Institute of Science Communication and Information Resources (NISCAIR), New Delhi, (NISCAIR/RHMD/Consult/-2011-12/1724/24).

Animals

A total of 132 Swiss mice divided in 22 different groups were employed in the present study. Each group comprised of a minimum of 6 animals. Young (3-4 months old) mice weighing around 20-25 g were procured from the Disease-Free Small Animal House of C.C.S. Haryana Agricultural University, Hisar. The experimental protocol was approved by the Institutional Animals Ethics Committee and the care of laboratory animals was taken as per the guidelines of CPCSEA, Ministry of Forests and Environment, Government of India (Reg. 0436).

Statistical analysis

All the results were expressed as mean $\pm$ Standard Error (SEM). Data were analyzed by one-way ANOVA followed by Dunnett's t-test.

RESULTS

Lagenaria siceraria juice (LSJ, 8%, v/v), when administered orally for 15 successive days did not show any significant change on the locomotor function of mice as compared to the control group. On the other hand, LSJ (4, 8 and 16%, v/v, p.o.), when administered for 15 successive days to mice diminished both, the immobility duration and despair behavior of mice ($p < 0.01$) in both the experimental models, i.e. Tail suspension test (TST) and Forced swim test (FST) respectively. The anti-depressant efficacy of ghiya (LSJ) was found to be comparable (Fig.1 and 2) to that of fluoxetine (5-HT reuptake inhibitor) and imipramine (Tricyclic anti-depressant). These findings suggest that *Lagenaria siceraria* juice possesses useful anti-depressant activity, which needs to be confirmed clinically. Prazosin (62.5 mg/kg i.p.), baclofen (10 mg/kg, i.p.), sulpiride (50 mg/kg, i.p.) and p-CPA (100 mg/kg, i.p.) *per se* increased significantly ($p < 0.01$) the immobility duration of mice as compared to the control group. Prazosin/baclofen/p-CPA /sulpiride, when administered on day 15, 45 min after the last dose of LSJ (8% v/v) reversed the diminished immobility duration observed with LSJ alone (Fig.3). LSJ (4, 8 & 16 % v/v), when administered to mice for 15 successive days, significantly ($p < 0.01$) reduced the brain MAO-A (nmol/mg protein) and MAO-B (nmol/mg protein) levels as compared to the control group. Furthermore, LSJ (Fig.4, 5 & 6) significantly ($p < 0.01$) reduced brain MDA levels as well (nmol/mg tissue).

DISCUSSION

Tail suspension test (TST) and forced swim test (FST) are commonly employed laboratory models to evaluate new anti-depressant medicines^{13, 14}. In TST, immobility reflects a state of helplessness, which can be reversed by drugs such as imipramine and fluoxetine effective clinically in human depression. Similarly in the FST, mice are forced to swim in a restricted space from which they cannot escape. This induces a state of behavioral despair in mice as reflected by increased immobility, which is similar to human depression¹⁵. Noradrenaline and serotonin levels are diminished considerably in patients suffering from depression. Since lauki contains high amounts of serotonin and fair amounts of noradrenaline¹², there is a possibility that the low levels of noradrenaline and serotonin observed in depressed patients are replenished by lauki, thereby producing anti-depressant effect. Furthermore, p-CPA (serotonin synthesis inhibitor) increased the duration of immobility in mice as expected and this effect of p-CPA was reversed by pre-treatment with *Lagenaria siceraria* juice. Thus, serotonin replenishment provided by lauki juice appears to be an important event in counteracting despair behavior produced due to inhibition of serotonin release. In addition to diminished levels of serotonin, reductions in the levels of noradrenaline are also observed in the patients suffering from depression¹⁶. Since lauki contains good amount of noradrenaline, adrenaline as well as serotonin, it can be looked upon as a promising anti-depressant. In the present study, prazosin (α_1 - adrenoceptor antagonist) produced increased immobility duration in mice probably through decreased noradrenergic activity due to blockade of α_1 - adrenergic receptors. However, this depressant action of prazosin was attenuated by pre-treatment of animals with lauki juice. Lauki juice administered to mice for 15 successive days produced a significant inhibition of monoamine-oxidase (MAO) activity. Since noradrenaline and serotonin are metabolized by MAO-A and MAO-B enzymes, inhibition of MAO enzyme (MAO-A as well as MAO-B) would lead to enhanced levels of both noradrenaline and

serotonin. Ghiya (lauki) is reported to possess powerful anti-oxidant activity³ as well. This fact was confirmed in the present study, wherein malondialdehyde (MDA) levels were significantly reduced by lauki juice indicating reduced generation of free radicals. Thus, *Lagenaria siceraria* juice appears to have produced its anti-depressant effect through i) inhibition of MAO-A and MAO-B enzymes, ii) reduction of malondialdehyde levels and iii) replenishment of noradrenaline and serotonin levels. However, the involvement of dopamine D₂- receptors, and GABA_B receptors in the antidepressant effect of *Lagenaria siceraria* juice (ghiya) cannot be ruled out, since both, sulpiride (a selective dopamine D₂-receptor antagonist), and baclofen (GABA_B agonist), reversed the diminished immobility time observed with LSJ alone.

CONCLUSION

The ghiya juice produced powerful and consistent anti-depressant effects in both the experimental models *viz* tail suspension test and forced swim test in the present study. It is remarkable to note that ghiya (lauki) juice contains high amounts of neurotransmitter serotonin and fair amounts of neurotransmitter noradrenaline, which play an important role in the pathology of depression. Furthermore, MAO inhibitory property and anti-oxidant activity possessed by lauki might be contributing favorably to its anti-depressant potential. Thus, it is worthwhile to investigate clinically the usefulness of ghiya (lauki) in managing depression.

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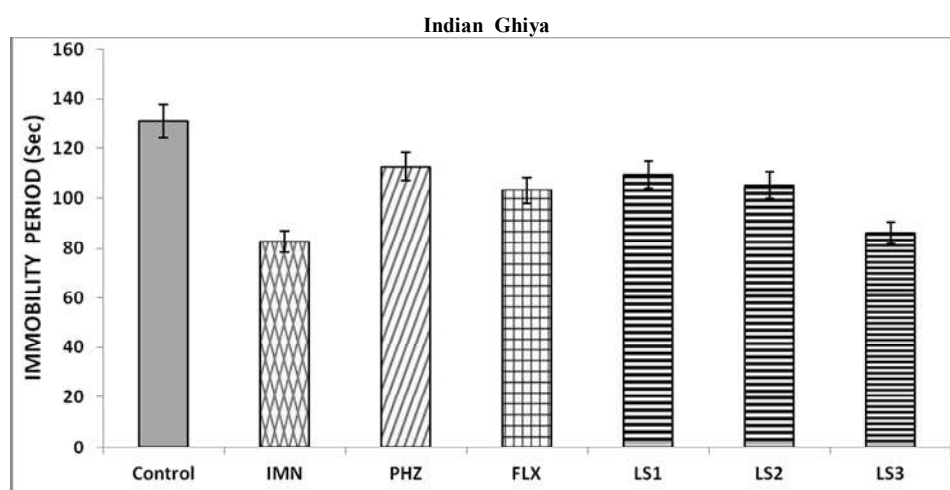


Figure1: Effect of *Lagenaria siceraria* juice (LSJ) on Immobility Duration of mice subjected to Tail Suspension Test
 FLX= Fluoxetine (20 mg/kg, p.o.), PHZ= Phenelzine (20 mg/kg, p.o.) and IMN= Imipramine (15 mg/kg, p.o.) were administered for 15 successive days.
 Values are in Mean $\pm$ SEM. (n=6)
 LS1 (LSJ 4% v/v), LS2 (LSJ 8% v/v), LS3 (LSJ 16% v/v)

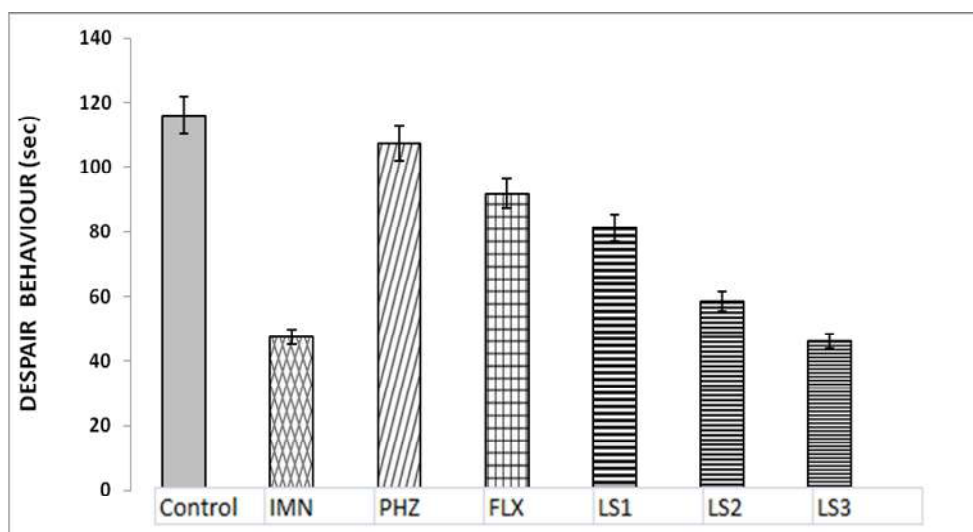


Figure 2: Effect of *Lagenaria siceraria* juice (LSJ) on Despair behavior of mice
 FLX= Fluoxetine (20 mg/kg, p.o.), PHZ= Phenelzine (20 mg/kg, p.o.) and IMN= Imipramine (15 mg/kg, p.o.) were administered for 15 successive days.
 LS1 (LSJ 4% v/v), LS2 (LSJ 8% v/v), LS3 (LSJ 16% v/v)

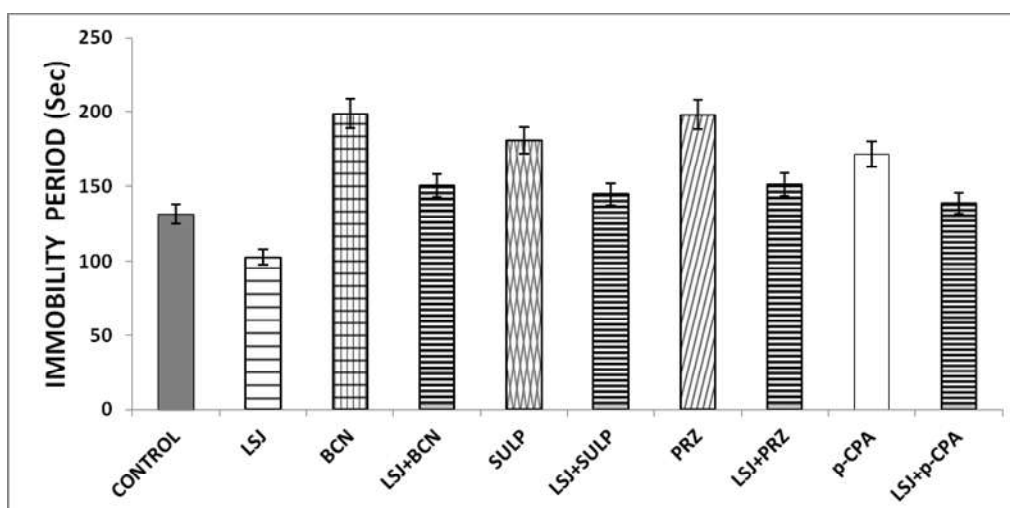


Figure 3: Effect of combination of *Lagenaria siceraria* juice (LSJ) with prazosin/baclofen/p-CPA/sulpiride on immobility duration of mice subjected to Tail Suspension Test
 Prazosin (62.5 mg/kg, i.p.), p-CPA (100 mg/kg, i.p.), baclofen (10 mg/kg, i.p) and sulpiride (50 mg/kg, i.p) were administered on 15th day,
 PRZ= Prazosin, BCN= Baclofen, p-CPA=para chlorophenyl alanine, SULP= Sulpiride

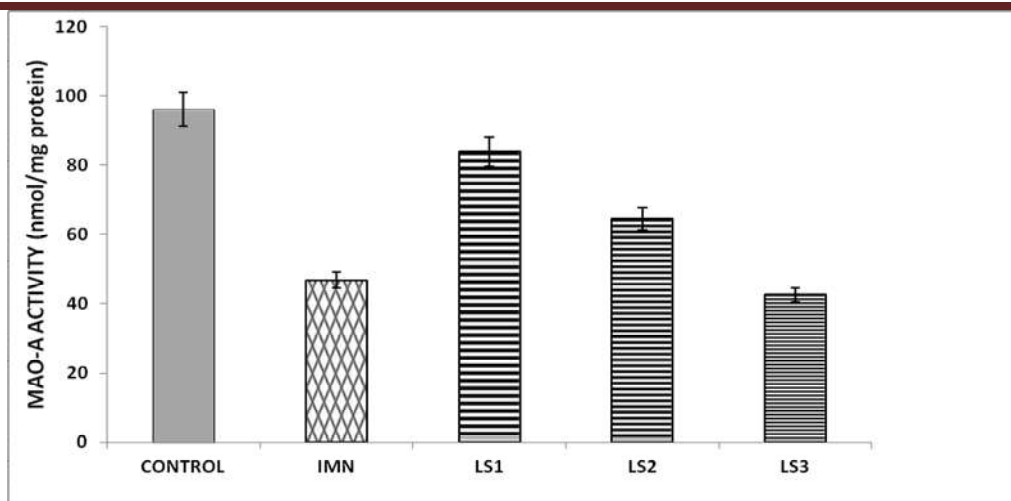


Figure 4: Effect of *Lagenaria siceraria* juice (LSJ) on MAO-A activity of mice

IMN= Imipramine (15 mg/kg, p.o.)

Values are in Mean $\pm$ SEM. (n=6)

LS1 (LSJ 4% v/v), LS2 (LSJ 8% v/v), LS3 (LSJ 16% v/v)

One way ANOVA followed by Dunnett's t-test

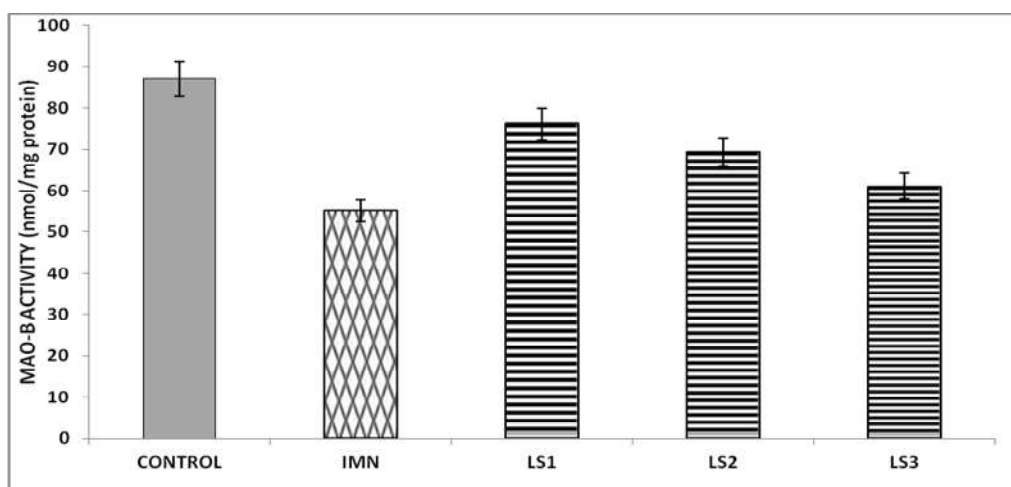


Figure 5: Effect of *Lagenaria siceraria* juice (LSJ) on MAO-B activity of mice

IMN= Imipramine (15 mg/kg, p.o.)

Values are in Mean $\pm$ SEM. (n=6)

LS1 (LSJ 4% v/v), LS2 (LSJ 8% v/v), LS3 (LSJ 16% v/v)

One way ANOVA followed by Dunnett's t-test

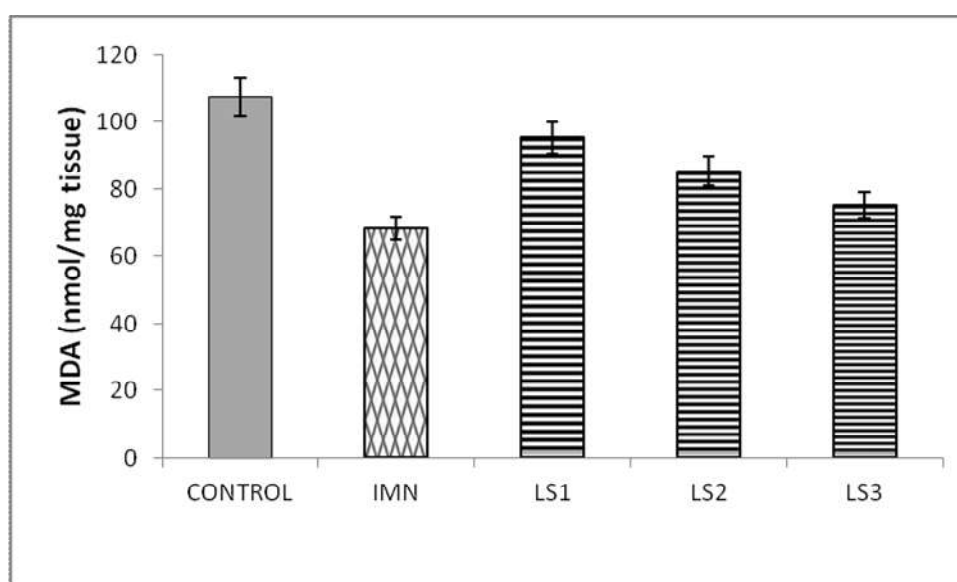


Figure 6: Effect of *Lagenaria siceraria* juice on MDA levels of mice

IMN= Imipramine (15 mg/kg, p.o.)

Values are in Mean $\pm$ SEM. (n=6)

LS1 (LSJ 4% v/v), LS2 (LSJ 8% v/v), LS3 (LSJ 16% v/v)