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Eat tomato a day to keep depression at bay

MILIND PARLE AND SUMAN MALIK
Pharmacology Division, Department Pharmaceutical Sciences, Guru Jambheshwar University of Science and Technology, HISAR (HARYANA), INDIA.

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Lycopersicon esculentum Mill (Solanaceae) popularly known as tomato, is a native of the western side of South America. Today, the United States of America, Russia, Italy, Spain, China, Egypt, Turkey and India are among the top selling commercial producers of tomatoes. Tomato leaves are used traditionally as antimicrobial agents. There are no reports in literature pertaining to CNS actions of *Lycopersicon esculentum* fruit. In the light of above, the present study was undertaken to test the antidepressant potential of *Lycopersicon esculentum* fruit juice. *Lycopersicon esculentum* juice (LEJ) was administered at various concentrations ranging from 5% to 20% v/v to Swiss mice, once daily for 15 successive days. The antidepressant activity was measured using forced swim test (FST) and tail suspension test (TST). The results showed that the LEJ significantly reduced the immobility time of mice in both FST and TST. Prazosin (62.5 mg/kg, i.p.) and p-CPA (100 mg/kg, i.p) significantly antagonized this reduction in immobility time. Furthermore, *Lycopersicon esculentum* juice inhibited the monoamine oxidase (MAO) enzyme and reduced significantly malondialdehyde (MDA) levels. These findings reveal the anti-depressant potential of tomato.

Key words : *Lycopersicon esculentum*, Anti-depressant, Forced swim test, Tail suspension test

INTRODUCTION

Mental depression is a chronic illness that affects a person's mood, thoughts, behaviour and physical health. Depression is a complex disorder of unknown aetiology, 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 dopamine (Gold *et al.*, 1998). However, most of the marketed anti-depressant drugs exhibit serious side-effects. Therefore, the use of alternative medicines is increasing worldwide. Various herbal drugs (e.g. St. John's wort) have shown promising results in treating experimental as well as clinical depression and many of these herbal drugs appear to be quite safe (Behnke *et al.*, 2002).

Lycopersicon esculentum Mill (Solanaceae) is commonly known as tomato. *Lycopersicon esculentum* is reported to possess several medicinal properties such as anti-diabetic (Soumya *et al.*, 2009), anti-allergic (Makoto *et al.*, 2004), anti-tumor (Canene *et al.*, 2007), anti-fungal (Baissac *et al.*, 2006), anti-oxidant (Ramandeep and Geoffrey, 2005), anti-hypertensive (Paran *et al.*, 2009), anti-clastogenic (Chandra Mohan *et al.*, 2003), anti-cytotoxic (Emmanuel *et al.*, 2009), anti-viral (Konowalchuk and Speirs, 1978), anti-coagulant (Kone-Bamba *et al.*, 1987), anti-edema (Yasukawa *et al.*, 1993) and anti-mutagenic (Eustolia *et al.*, 2009). Tomato contains several pharmacologically active phytochemicals such as chlorogenic acid, rutin, naringenin (Makoto *et al.*, 2004), lycopene (Canene *et al.*, 2007), tomatoside-A (Baissac *et al.*, 2006), flavonoids, lycopene, ascorbic acid (Ramandeep and Geoffrey, 2005), bergapten and tomatin (Soumya *et al.*, 2009). Furthermore, tomato also contains high amounts of flavonoids (Gwénaëlle *et al.*, 2003) and neurotransmitters such as serotonin (Feldman and Lee, 1985), dopamine, adrenaline and noradrenaline (Mariela and Christina, 1997). However, there is no scientific evidence for the therapeutic potential of tomato in neuropsychiatric disorders. Since serotonin and noradrenaline levels fall considerably in depression, we were interested to investigate the usefulness of tomato in depression, since tomato is reported to contain high amounts of serotonin and fair amounts of adrenaline and noradrenaline.

The present study was undertaken to explore the anti-depressant potential of *Lycopersicon esculentum* juice (LEJ) using forced swim test and tail suspension test. An attempt has also been made to determine the underlying mechanism of action of LEJ by co-administration of agents modulating noradrenaline, serotonin and malonaldialdehyde activities.

MATERIALS AND METHODS

Plant material:

The fresh tomatos (*Lycopersicon esculentum*) were purchased from local market of Hisar and got authenticated from Raw Materials Herbarium and Museum, National Institute of Science Communication and Information Resources, New Delhi. Different concentrations of *Lycopersicon esculentum* juice (5, 10, 20%, v/v, p.o.) *per se* was administred to mice at the dose rate of 1 ml/100g body weight for a duration of 15 days.

Animals:

A total of 126 Swiss mice divided in 21 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 (Registration number 0436).

Statistical analysis:

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

RESULTS AND DISCUSSION

The results are summarized below according to objectives of the study:

Locomotor activity:

Lycopersicon esculentum juice (10%, v/v) administered orally for 15 successive days did not show any significant change in the locomotor function of mice (706.33 +21.093) as compared to the control group (733.33 +29.095).

Effects of Lycopersicon esculentum juice (LEJ) on immobility periods in TST and FST:

Tail suspension test (TST) and forced swim test (FST) are commonly employed to evaluate new anti-depressant medicines (Porsolt *et al.*, 1978; Steru *et al.*, 1985). 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 depression (Willner, 1984). LEJ (5, 10 and 20%, v/v, p.o.) *per se* administered for 15 successive days to mice decreased the duration of immobility significantly ($p<0.01$) in a dose-dependent manner in both the experimental models (TST amd FST). The antidepressant efficacy of LEJ was found to be comparable to that of fluoxetine (5-HT reuptake inhibitor) and imipramine (Tricyclic anti-depressant) administered for 15 successive days (Fig.1 and 2).

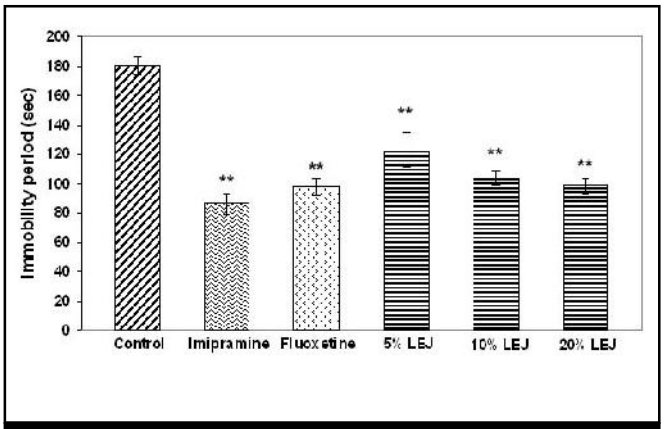

Fig. 1 : Effects of *Lycopersicon esculantum* on immobility period in tail suspension test.Values are in mean ± SEM. (n=6). ** denotes p<0.01 as compared to control group
LEJ = *Lycopersicon esculantum* juice

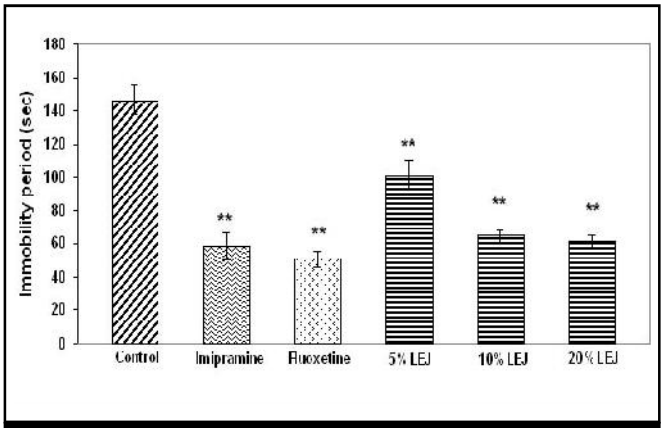

Fig. 2 : Effects of *Lycopersicon esculantum* on immobility period in forced swim test.
Values are in mean ± SEM. (n=6). ** denotes p<0.01 as compared to control group
LEJ = *Lycopersicon esculantum* juice

Effect of combination of Lycopersicon esculentum juice (10% v/v) with prazosin/p-CPA on immobility periods using TST:

Prazosin (62.5 mg/kg i.p.) and p-CPA (100 mg/kg, i.p.) *per se* increased significantly the immobility period of mice as compared to the control group. Pretreatment of mice with prazosin/p-CPA significantly ($p<0.05$) and $p<0.01$) reversed the diminished immobility time observed with LEJ (Fig.3) using TST.

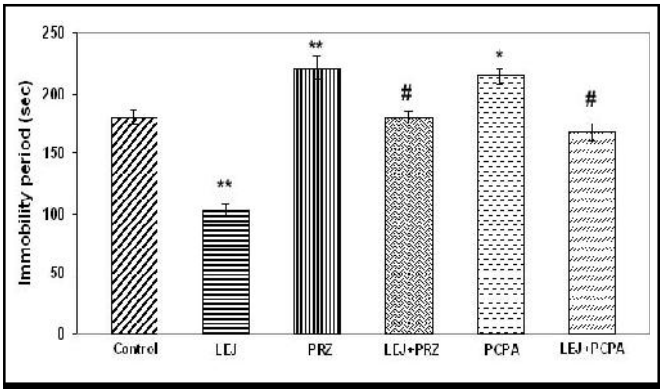

Fig. 3 : Effect of combination of LEJ (10% v/v) with prazosin/ p-CPA on immobility period of mice in tail suspension test. Values are in mean ± SEM. (n = 6). * denotes p<0.05 when compared to control group, **denotes p < 0.01 when compared to control group and # denotes p < 0.01 when compared to LEJ alone. LEJ = *Lycopersicon esculantum* juice, PRZ= Prazosin & PCPA= para chlorophenyl alanine

Effect of Lycopersicon esculentum juice (10% v/v) on brain monoamine oxidase (MAO) activity and malondialdehyde (MDA) levels:

LEJ (10% v/v) administered to mice for 15 successive days, significantly ($p<0.01$) reduced the brain MAO-A (25.166 ± 2.058 U/g protein) and MAO-B (35.833 ± 2.023 U/g protein) levels as compared to the control group. Furthermore, LEJ (Fig.4 ,5 and 6) produced significant ($p<0.01$) decrease in brain MDA levels (64.166 ± 2.833 nmol/g tissue) as compared to the control mice (108.5 ± 4.877 nmol/ g tissue.

Anti-depressant potential of *Lycopersicon esculentum* was tested in mice employing two standard experimental models *viz.*, Forced swim test (FST) and Tail suspension test (TST). The index of depression in these experimental models is taken as the immobility duration over a specific period of time. This immobility reflects helplessness or despair behaviour of animals equivalent to depression in human beings. In the present study, different concentrations of *Lycopersicon esculentum* juice (5, 10 and 20% v/v, p.o.) *per se* were administered for 15 successive days to mice. *Lycopersicon esculentum* juice decreased significantly

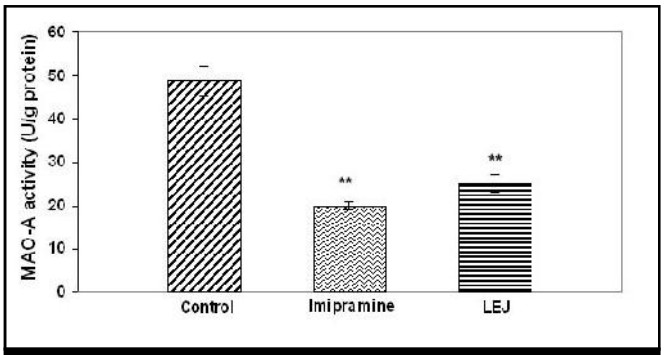

Fig. 4 : Effect of LEJ (10% v/v) on MAO-A activity. Values are in mean ± SEM (n =6). ** denotes p < 0.01 when compared to control group. LEJ = *Lycopersicon esculantum* juice

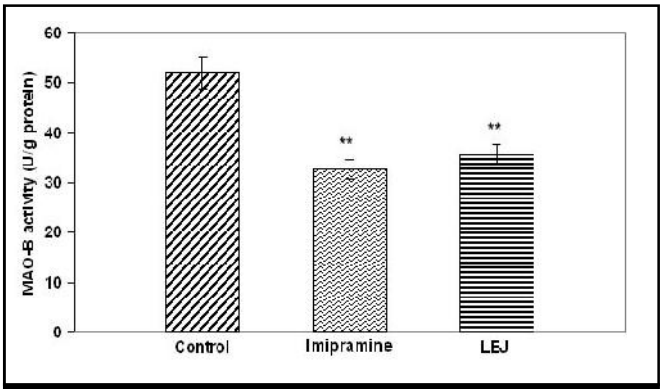

Fig. 5 : Effect of LEJ (10% v/v) on MAO-B activity. Values are in mean ± SEM (n =6). ** denotes p < 0.01 when compared to control group. LEJ = *Lycopersicon esculantum* juice

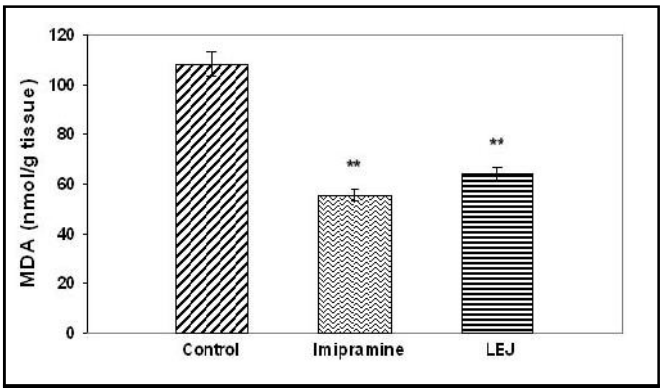

Fig. 6 : Effect of LEJ (10% v/v) on MDA levels. Values are in mean ± SEM (n =6). ** denotes p < 0.01 when compared to control group. LEJ = *Lycopersicon esculantum* juice.

the immobility duration in a dose-dependent manner in both the experimental models. This effect of LEJ was comparable to imipramine (Tricyclic anti-depressant) and fluoxetine (5-HT reuptake inhibitor). These findings suggest that *Lycopersicon esculentum* juice possesses useful anti-depressant activity, which needs to be confirmed clinically.

Noradrenaline and serotonin levels are diminished considerably in patients suffering from depression (Maas, 1975). Since tomato contains high amounts of serotonin (Feldman and Lee, 1985) and fair amounts of noradrenaline (Mariela and Christina, 1997), there is a possibility that the low levels of noradrenaline and serotonin observed in depression are replenished by tomato, 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 *Lycopersicon esculentum* juice. Thus, serotonin replenishment provided by tomato juice appears to be an important event in counteracting despair behaviour 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 depression (Cooper and Kelly, 2000). Since tomato contains good amount of noradrenaline, adrenaline as well as serotonin, it can be looked as a promising anti-depressant. In the present study, prazosin (a 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 tomato juice.

Tomato juice and imipramine (standard anti-depressant) both 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. Tomato is reported to possess powerful anti-oxidant activity (Ramandeep and Geoffrey, 2005). This fact was confirmed in the present study, wherein malondialdehyde (MDA) levels were significantly reduced by tomato juice indicating reduced generation of free radicals responsible for producing neuronal damage.

Thus, *Lycopersicon esculentum* juice appears to have produced its anti-depressant effect through i) inhibition of MAO-A and MAO-B ii) reduction of malondialdehyde levels iii) replenishment of noradrenaline and serotonin. *Lycopersicon esculentum* juice may be exploited clinically for the management of depressive disorders.

Conclusion:

The tomato 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 tomato 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 tomato might be contributing favorably to the anti-depressant potential. Thus, it is worthwhile to investigate clinically the usefulness of tomato in managing depressive disorders.

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