CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES
SJIF Impact Factor: 7.187

Available online at: http://www.iajps.com *Research Article*

PHARMACOLOGICAL PROFILE, FORMULATION AND COMPARISION OF CITRULLUS LANATUS AS AN ANTI-DEPRESSANT

Humera Mohammadi[1], Adiba Afreen[2], Dr. Noorunnisa Begum[3], Lateef unnisa[4]

[1]Associate Professor (Department of Pharmacology) – Shadan College of Pharmacy, Peerancheru, Hyderabad 500091, Telangana India

[2]Associate Professor (Department of Pharmacology) – Shadan College of Pharmacy, Peerancheru, Hyderabad 500091, Telangana India

[3]Assistant Professor (Pharm D) – Shadan College of Pharmacy, Peerancheru, Hyderabad 500091, Telangana India

[4]M. Pharmacy (Pharmaceutical Chemistry)

Article Received: October 2021 **Accepted:** October 2021 **Published:** November 2021

Abstract:

Background: *Depressed mood is a feature of some psychiatric syndromes such as major depressive disorder, but it may also be a normal reaction to life events such as bereavement, a symptom of some bodily ailments or a side effect of some drugs and medical treatments.*

Objective: *To study systemic chemical investigation to be carried out on Citrullus lanatus as antidepressant and compared with standard drug .*

Methods: *Male Wistar rats weighing 250-300g were housed in groups of 4 and 6 animals. The animals were acclimatized for a period of 7 days before the study. The animals were forced to swim in a glass cylinder measuring 25cm height, 12cm diameter containing water at room temperature to a depth of 15cm. After an initial 2 minute period of vigorous activity, each animal assumed a typical immobile posture. The mouse was considered immobile when it remained floating in the water without struggling, making only minimum movements of its limbs necessary to keep its head above water. The total duration of immobility was recorded during last 4 minutes of total 6 minute test.*

Results: *In forced swim test a significant decrease in the duration of immobility was seen with standard drug fluoxetine and all test dose of CLE as compared to control. However the immobility time of higher dose of CLE was comparable with that of standard drug. It was observed that the extract shows dose dependent effect in immobility time. With increase of dose the immobility time decreased. Thus, it can be said that CLE shows anti-depressant effect.*

In Tail Suspension Test there was a significant decrease in duration of immobility with that of standard drug when compared to control. The immobility time decreased with the increase of dose. The immobility time of standard drug and that of CLE higher extract are almost same showing the efficiency of the extract in its anti-depressant activity.

Conclusion: *The antidepressant activity is attributed due to the presence of polyphenols, flavanoids in the extract. The effective components of Citrullus lanatus that have antidepressant-like effect includes S-adenosylmethionine, dopamine, b vitamins, 5-hydroxytryptophan (5-htp) and tryptophan. Hence its effect is almost similar to that of standard drug.*

Keywords: *S-adenosylmethionine, dopamine, b vitamins, 5-hydroxytryptophan, tryptophan*

Corresponding author:

Humera Mohammadi,

Associate Professor,
Department of Pharmacology,
Shadan College of Pharmacy,
Contact Number: 6303858566,
Email Address: humeramohammadi53@gmail.com

QR code

Please cite this article in press Humera Mohammadi et al, ***Pharmacological Profile, Formulation And Comparison Of Citrullus Lanatus As An Anti-Depressant,*** *Indo Am. J. P. Sci, 2021; 08(11).*

INTRODUCTION:

Sadness and grief are normal human emotions. We all have those feelings from time to time, but they usually go away within a few days. Depression[1] is a state of low mood and aversion to activity that can affect a person's thoughts, behavior, feelings and sense of well-being. People with depressed mood can feel sad, anxious, empty, hopeless, helpless, worthless, guilty, irritable, ashamed or restless. They may lose interest in activities that were once pleasurable, experiences overeating or loss of appetite, have problem in concentrating, remembering details or making decisions, and may contemplate, attempt or commit suicide. Insomnia, excessive sleeping, fatigue, aches, pains, digestive problems or reduced energy may also be present. Depressed mood is a feature of some psychiatric syndromes but it may also be a normal reaction to life events such as bereavement, a symptom of some bodily ailments or a side effect of some drugs and medical treatments.

Major depression is something more. It's a period of overwhelming sadness. It involves a loss of interest in things that used to bring pleasure. Those feelings are usually accompanied by other emotional and physical symptoms. Untreated, depression can lead to serious complications that put your life at risk. Fortunately, most people can be effectively treated. When depression lasts two years or more, it is called persistent depressive disorder. A less common type of depression is called bipolar disorder, or manic-depressive illness. Bipolar disorder involves cycles of depression alternating with extreme highs, or manias.Specific circumstances can trigger other forms of depression.

In seasonal affective disorder [2] (SAD) mood is affected by sunlight. People are more likely to be depressed during winter, when there's less sunshine. Many new mothers go through something called the baby blues. It's caused by hormonal changes following childbirth, lack of sleep, and everything that goes along with taking care of a new baby.

Symptoms include mood swings, sadness, and fatigue. These feelings usually pass within a week or two. When they drag on longer and escalate, it may be a case of postpartum depression.

According to the National Institute of Mental Health (NIMH), about 10 to 15 percent of women develop postpartum depression. Untreated, it can be dangerous for mother and baby. When major depression or bipolar disorder are accompanied by hallucinations, delusions, or paranoia, it's called psychotic depression. About 20 percent of people with major depressive disorder develop psychotic symptoms, according to the National Alliance on Mental Illness (NAMI).

Depression is a major cause of morbidity worldwide. The relative increase in occurrence is related to pubertal development rather than chronological age, reaches adult ratios between the ages of 15 and 18, and appears associated with psychosocial more than hormonal factors. People are most likely to suffer their first depressive episode between the ages of 30 and 40, and there is a second, smaller peak of incidence between ages 50 and 60. The risk of major depression is increased with neurological conditions such as stroke, Parkinson's disease, or multiple sclerosis and during the first year after childbirth. It is also more common after cardiovascular illnesses and is related more to a poor outcome than to a better one. Studies conflict on the prevalence of depression in the elderly, but most data suggest there is a reduction in this age group. Depressive disorders are more common to observe in urban than in rural population and the prevalence is in groups with stronger socioeconomic factors i.e. homelessness.

States with higher rates of depression also show high rates of other negative health outcomes such as obesity, heart disease, and stroke. Its symptoms can be disabling and its effects pervasive, impacting on not only the individual patient but also on their families and the wider society. In spite of availability of large number of anti-depressant drugs like MAO inhibitors, SSRIs, SNRIs depression is a major medical problem[3].

Because these drugs when administered may cause many side effects hence Natural medicines are being used for treatment which will have fewer side effects and will be equally effective as synthetic drugs. Now as a global health issue, depression awareness, diagnosis, and treatment are matters of crucial significance in building a healthier and a happier world.

Citrullus lanatus is a plant species in the family Cucurbitaceae, a vine-like flowering plant originally from WestAfrica.

It is cultivated for its fruit. The subdivision of this species into two cultivars, watermelons (*Citrullus lanatus* (Thunb.) var. *lanatus*) and citron melons (*Citrullus lanatus* var. *citroides* (L. H. Bailey) Mansf.), originated with the erroneous synonymization of *Citrullus lanatus* (Thunb.) Matsum. & Nakai and *Citrullus vulgaris* Schrad. by L.H.Bailey in 1930.

Molecular data including sequences from the original collection of Thunberg and other relevant type

material, show that the sweet dessert watermelon (*Citrullus vulgaris* Schrad.) and the bitter wooly melon *Citrullus lanatus* (Thunb.) Matsum. & Nakai are not closely related to each other.

Since 1930, thousands of papers have misapplied the name *Citrullus lanatus* (Thunb.) Matsum. & Nakai for the dessert watermelon, and a proposal has therefore been submitted to conserve the name with this meaning.

MATERIALS AND METHODS:

Animals and husbandry:

The experimental protocol was approved by the Institutional Animal Ethics Committee (IAEC)

Male Wistar rats weighing 250-300g were obtained from the Animal House of the Department of Pharmacology. They were relocated from the Animal Rearing Section to the Experimental Study Section of the Animal House a week before the study to make them adapt to the new environment. They were housed in groups of 4 and 6 animals in each group in stainless steel cages with wood shavings as the bedding material and a wire screen top. The cages were adequately ventilated and kept at a room temperature and relative humidity of 24-28ºC and 60-70% respectively, with a natural light-dark cycle. Good hygiene was maintained.

They were fed with commercially available mouse normal pellet diet and water was allowed ad libitum. The animals were acclimatized for a period of 7 days before the study

Drugs and chemicals

- Distilled water
- Aqueous extract of *Citrullus lanatus*
- Fluoxetine
- Certain Chemicals for photochemical screening

The standard antidepressant drug fluoxetine was obtained from our institutional pharmacy. The test drug *Citrullus lanatus* was standardized and provided by Natural Remedies Pvt. Ltd

Preparation of *Citrullus lanatus* extract[4]

Plant material and preparation of extract[4,5]

The test drug *Citrullus lanatus* fruit was provided by Natural Remedies Pvt. Ltd

The fruit was washed, and then the exocarp was removed using a sterile knife. After which, the fruit juice was extracted using a manual juice extractor. The resultant juice collected was retained in a sterile vessel and stored at 4°C till used.

Acute toxicity study

Acute oral toxicity studies: Acute oral toxicity study was carried out for aqueous extracted *Citrullus lanatus* using Acute Toxic Class Method as described in OECD (Organization of Economic Co-operation and Development) Guidelines No. 423.

The extract was safe up to a dose of 2,000 mg/kg body weight.

PRELIMINARY PHYTOCHEMICAL SCREENING:[6,7]

Citrullus lanatus extract were subjected to phytochemical screening in accordance with the standard procedure.

1. Test for alkaloids

a.Test by Dragendorff reagent(Potassium-bismuth-iodide solution): Alkaloids give reddish-brown precipitate with this reagent.

b.Test by Mayer reagent (Potassium-mercuric-iodide solution): Alkaloids gives cream colour precipitate with this reagent.

c.Test by Wagner reagent (iodine-potassium-iodide solution): Alkaloids give Brown colour precipitate with this reagent.

d.Test by Hager reagent (Saturated solution of picric acid): Alkaloids give yellow colour precipitate with this reagent.

2.Test by Tannic acid:

Alkaloids gives buff colour precipitate with this acid.

3.Test for phenols

When the extract were treated with neutral ferric chloride solution, the appearance of violet color indicates the presence f phenols

When the extracts were treated with 10% sodium chloride solution, the appearance of cream color indicates the presence of phenols

4. Test for flavanoids

The ethanol extract (5 ml) was added to a concentrated sulphuric acid (1 ml) and 0.5g of Mg. A pink or red

coloration that disappear on standing (3 min) indicates the presence of flavonoids.

5.Test for tannins

Solution of tannins precipitates gelatin and alkaloids.

Tannins are precipitated by salts of copper, tin and lead

They are precipitated by strong potassium dichromate solution or chromic acid solution.

They show color reaction with iron salts ferric chloride gives bluish black or brownish green color potassium ferric cyanide with ammonia gives deep red color.

Gold beaters skin test.

Tannins are precipitated by 2% solution of phenazone. The tannin solution being prepared with sodium acid phosphate.

6. Test for saponins

To 1 ml of aqueous extract was added few volume of distilled water in a test tube. The solution was shaken vigorously and observed for a stable persistent froth for 20 min.

7. Test for carbohydrates

A.Molisch's test: The test is positive with soluble as well as insoluble carbohydrates.it consists of treating compounds with alpha-naphthol and sulphuric acid which gives purple color.

B.Reduction of Fehlings solution: To the solution of carbohydrates equal quantity of fehlings soln A and B is added.after heating brick red ppt is obtained.

8. Test for protein

A.Biuret's Test: When the extract were treated with copper sulphate solution, followed by the addition of sodium hydroxide solution, appearance of violet color indicates the presence of proteins.

B.Millon's Test: When the extract is treated with millons reagent, appearance of pink color indicates the presence of proteins.

9: Test for terpenes:

When the extract was treated with tin and thionyl chloride, appearance of pink color indicates the presence of terpene.

10.Test for glycosides:

When a extracts is mixed with the glacial acetic acid and few drops of chloride solution was added, followed by the addition of concentrated sulphuric acid, formation of red ring at the junction of two liquids indicates the presence of glycosides.

10)Test for sterols

Sterols were sought by the reaction of Liebermann.

Ten (10 ml) ml of extract was evaporated. The residue was dissolved in 0.5 ml of hot acetic anhydride, we add 0.5 ml of chloroform to the filtrate. Treate with the reagent of Libermann Burchardt. The appearance of blue-green ring at the interphase shows positive reaction.

11)Test for amino acids

a)Ninhydrin test

Amino acids react with ninhydrin (triketohydrindene hydrate), a powerful oxidizing agent to give a purple colored product (diketohydrin) termed Rhuemann's purple.

All primary amines and ammonia react similarly but without the liberation of carbon dioxide.

Besides amino acids, other complex structures such as peptides, peptones and proteins also react positively when subjected to the ninhydrin reaction.

b) Test for tyrosine and tryptophan

Xanthoproteic acid test

Aromatic amino acids, such as tyrosine and tryptophan, respond to this test.

In the presence of concentrated nitric acid, the aromatic phenyl ring is nitrated to give yellow colored nitro-derivatives. At alkaline pH, the color changes to orange due to the ionization of the phenolic group.

Millon's test:

Phenolic amino acids such as Tyrosine and its derivatives respond to this test.

Compounds with a hydroxybenzene radical react with Millon's reagent to form a red colored complex.

Millon's reagent is a solution of mercuric sulphate in sulphuric acid.

c)Test for methionine:[8,9]

Folin's McCarthy Sullivan Test

Addition of sodium nitroprusside [Na2Fe (CN)5NO] to an extract followed by the acidification of the reaction yields a red colour.

This reaction also forms the basis for the quantitative determination of methionine.

12)Test for Triterpenoids:[8,9]

Liebermann Burchard test:

Extract was mixed with few drops of acetic anhydride, boiled and cooled. Concentrated sulphuric acid was then added from the sides of the test tube and observed for the formation of a brown ring at the junction of two layers. the formation of deep red color in the lower layer would indicate a positive test for triterpenoids.

Dosing of experimental animals:

Doses of Citrullus lanatus in this study (i.e. dose1 and dose2) were selected based on a preliminary study and acute toxicity study conducted.

Wistar rats were dosed and Individual dose volumes were calculated based on the animal's most recent recorded body weight. The oral route of administration was used because it is the intended human exposure route.

Experimental procedure:

For studying the effect of extract of *Citrullus lanatus* on animals, which were grouped into 4 containing 6 animals in each group.

Grouping and drug treatment

The animals were grouped into 4 different groups, each containing 6 animals, according to different tests of antidepressant activity as follows:

Group 1: Distilled Water 10 ml/kg [Normal]

Group 2: Diseased State + Fluoxetine 20 mg/kg [Standard for Locomotor Activity testing, FST and TST.]

Group3: Diseased State + Aqueous extract of Citrullus lanatusDose1.

Group4: Diseased State + Aqueous extract of Citrullus lanatus Dose2 .

Group 2: served as test group for locomotor activity testing, FST and TST respectively. Fluoxetine (reference standard drugs) is dissolved in distilled water and administered via i.p. route half an hour before each test. Test groups were treated with aqueous extract p.o. one hour prior to the test.

MODELS FOR ASSESMENT OF ANTI DEPRESSANT ACTIVITY:[9,10]

1. FORCED SWIMMING TEST(FST)
2. TAIL SUSPENSION TEST (TST)

1.Forced Swimming Test(FST)

Principle:

"Behavioral despair" is a standard proposed model to test for antidepressant activity. It is suggested that mice or rats forced to swim in a restricted space from which they cannot escape are induced to a characteristic behaviour of immobility. This behaviour reflects a state of despair which can be reduced by agents which are therapeutically effective in human depression.

Procedure:

The animals were forced to swim in a glass cylinder measuring 25cm height, 12cm diameter containing water at room temperature to a depth of 15cm. After an initial 2 minute period of vigorous activity, each animal assumed a typical immobile posture.

The mouse was considered immobile when it remained floating in the water without struggling, making only minimum movements of its limbs necessary to keep its head above water. The total duration of immobility was recorded during last 4 minutes of total 6 minute test. After 6 min mouse was taken out, dried with a towel. The water is changed after each test because urine and the other chemicals released by the first mouse will affect the swimming pattern of the next mouse.

The following behaviours were recorded during the last 4 min

- Immobility: floating in water without swimming.
- Swimming: active movements of extremities and circling in the container.
- Climbing: active movements of forelimbs on the container wall.

Groups 1 to 4 were used for this model. The procedures were conducted after 1 hour of administrating the drug orally to animals.

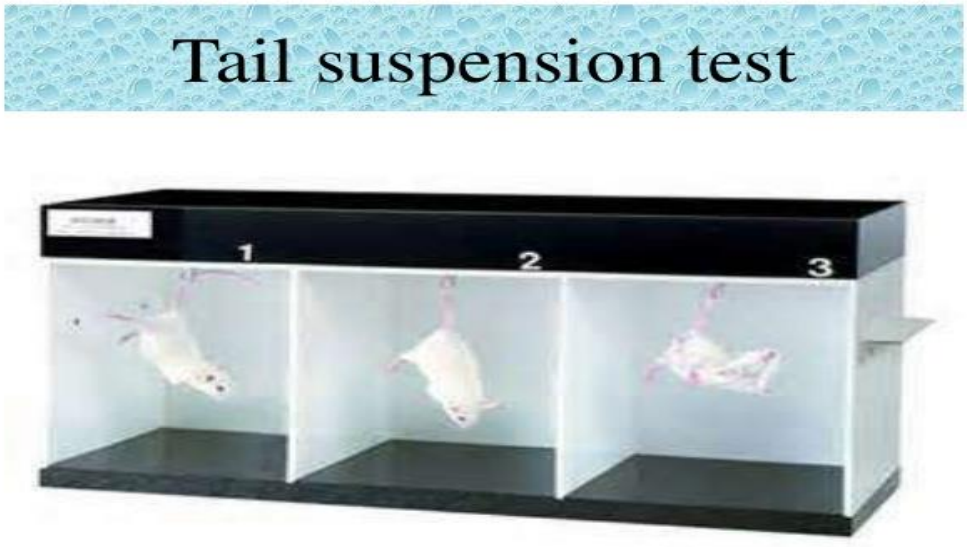
2. TAIL SUSPENSION TEST (TST)

Principle:

This test has been a facile means of evaluating potential antidepressants. The immobility displayed by mice when subjected to an unavoidable and inescapable stress has been hypothesized to reflect "behavioral despair" which in turn may reflect depressive disorders in humans. Clinically effective antidepressants reduce the immobility that mice display after active and unsuccessful attempts to escape when suspended by the tail.

Procedure:

Animals were suspended upside down on a metal rod at a height of 55 cm from the ground with the help of an adhesive tape placed approximately 1 cm from the tip of the tail. Initially the animals tried to escape by making vigorous movements but when unable to escape became immobile. The animal was considered immobile when it did not show any movement of body and hanged passively. The total duration of immobility was noted during last 4 minutes of 6 minute period. Groups 1 to 4 is used again for this model after one week. The procedures were conducted after 1 hour of administrating the drug orally to animals.



Statistical Analysis: The data obtained was analyzed using one-way ANOVA followed by Dunnette's multiple comparison test. $P < 0.05$ was considered significant.

OBSERVATION AND RESULTS:

Citrullus lanatus, being the extract with the highest number of phytochemicals, was selected and subsequently used as the extract in this study. *Citrullus lanatus* are known to contain bioactive compounds such as cucurbitacin, triterpenes, sterols and alkaloids. The amino-acid citrulline had been extracted from watermelon and analyzed. Watermelon with red flesh is a significant source of lycopene. Every aspect of the fruit of watermelon has nutritional value, including the rind and the seeds.

Citrullus lanatus extract was also examined for the presence of carbohydrates, flavanoids, proteins, saponins, glycosides, and tannins according to standard procedures.

Table 1: Evaluation of Phytochemicals

S.NO	NAME OF THE PHYTOCHEMICALS	RESULT
1	ALKOLOIDS	PRESENT
2	PHENOLS	PRESENT
3	FLAVONOIDS	PRESENT
4	TANNINS	PRESENT
5	SAPONINS	PRESENT
6	GLYCOSIDES	PRESENT
7	STEROLS	PRESENT
8	CARBOHYDRATES	PRESENT
9	PROTEINS	PRESENT
10	TRITERPENES	PRESENT
11	AMINOACIDS	PRESENT

EVALUATION OF ANTI DEPRESSANT ACTIVITY:

The behavioral despair model was performed in order to investigate the ability of this natural drug in the treatment of depression. The results obtained from FST and TST clearly reveals the fact that this drug is potentially quite useful in cases of depression.

FORCED SWIMMING TEST:

Effects of *Citrullus lanatus* extract on forced swim test showing swimming time

Table 2: Forced Swimming Test

Group	Treatment	Dose	Swimming Time (In Seconds)
I	Distilled Water	10ml/kg	70±3.96
II	Fluoxetine	20mg/kg	125±2.45
III	CLE-I	300mg/kg	100±3.45
IV	CLE-II	600mg/kg	120±6.97

CLE-I *Citrullus lanatus* extract of dose-I

CLE-II *Citrullus lanatus* extract of dose-II

In forced swim test increase in duration of swimming time was seen with that of standard drug fluoxetine as compared to control and different extract of CL. The swimming time was significantly more and was nearer to that of standard drug of higher dose of CLE .with increase of extract dose swimming time increase. From the above observation it can be said that CLE shows anti-depressant effect.

Effects of *Citrullus lanatus* extract on forced swim test showing climbing time:

Table 3: Effects of *Citrullus lanatus* extract on forced swim test showing climbing time

GROUP	TREATMENT	DOSE	CLIMBING TIME(SECONDS)
I	DISTILLED WATER	10ml/kg	30±3.96
II	FLUOXETINE	20mg/kg	48±3.24
III	CLE-I	300mg/kg	41±4.24
IV	CLE-II	600mg/kg	45(+or-)±6.87

In forced swim test increase in duration of climbing time was seen with that of standard drug fluoxetine as compared to control and different extract of CL. The climbing time was significantly more and was nearer to that of standard drug of higher dose of CLE with increase of extract dose climbing time increase. From the above observation it can be said that CLE shows anti-depressant effect.

Effects of *Citrullus lanatus* extract on forced swim test showing immobility time:

Table 4: Effects of *Citrullus lanatus* extract on forced swim test showing immobility time

GROUPS	TREATMENT	DOSE	IMMOBILITY TIME(SECONDS)
I	DISTILLED WATER	10ml/kg	180±3.96
II	FLUOXETINE	20mg/kg	125±2.45
III	CLE-I	300mg/kg	138±3.45
IV	CLE-II	600mg/kg	129±6.97

In forced swim test a significant decrease in the duration of immobility was seen with standard drug fluoxetine and all test dose of CLE as compared to control. However, the immobility time of higher dose of CLE was comparable with that of standard drug. It was observed that the extract shows dose dependent effect in immobility time. With increase of dose the immobility time decreased. Thus it can be said that CLE shows anti-depressant effect.

TAIL SUSPENSION TEST:

Effects of *Citrullus lanatus* extract on tail suspension test showing immobility time

Table 5: Effects of *Citrullus lanatus* extract on tail suspension test showing immobility time

GROUP	TREATMENT	DOSE	IMMOBILITY TIME(SECONDS)
I	DISTILLED WATER	10ml/kg	100±3.61
II	FLUOXETINE	20mg/kg	63±5.22
III	CLE-I	300mg/kg	78±5.63
IV	CLE-II	600mg/kg	69±5.66

In Tail Suspension Test there was a significant decrease in duration of immobility with that of standard drug when compared to control. The immobility time decreased with the increase of dose. The immobility time of standard drug and that of CLE higher extract are almost same showing the efficiency of the extract in its anti-depressant activity.

Statistical analysis-one way ANOVA followed by Dunnetts 't' test, $P<0.05$. Results are expressed as mean ± SEM obtained from six animal

DISCUSSION:

The present study evaluated the antidepressant activity of aqueous extract of fruits of *Citrullus lanatus* in two different animal models of depression.

- TAIL SUSPENSION TEST
- FORCED SWIM TEST

Both these methods are widely used for screening antidepressant drugs. These tests are quite sensitive and relatively specific to all major classes of antidepressants like tricyclics, selective serotonin reuptake inhibitors (SSRIs), monoamine oxidase inhibitors (MAOIs) and atypical antidepressants.[11] It has been argued that tail suspension is less stressful than forced swim test and has greater pharmacological sensitivity. Reduction in duration of immobility showed that the aqueous extract of fruit on administration has antidepressant effect similar to standard drug like fluoxitine.

To sum up, the present study has shown that the aqueous extract of fruits at a dose of 300mg/kg, 600 mg/kg significantly reduced the duration (time) of immobility of animals as compared to the normal in both tail suspension test and forced swim test of depression, showing that in both the doses, it has significant antidepressant activity. Both the tests showed consistent results in terms of reduction in the duration of immobility.

Exact mechanisms underlying the antidepressant action cannot be concluded at the moment due to the presence of large number of phytochemicals in the extract. However, the antidepressant activity may be attributed to the presence of polyphenols, flavanoids in the extract. Another possible mechanism of action is the attenuation of oxidative stress produced during depression, by the polyphenols and tannic acid present in extract. aqueous extract contains lycopene has been reported to possess cytoprotective effects on account of its antioxidant activity by reducing lipid peroxidation and also significantly scavenges superoxide as well as inhibits its generation. Aqueous extract of fruits of has been found to be potent antioxidants in vitro.[11]

S -Adenosylmethionine (SAMe):

It is a natural product that contains high level of S-Adenosylmethionine (SAMe).SAMe is an amino acid derivative that occurs naturally in all cells. It plays a role in many biological reactions by transferring its methyl group to DNA, proteins, phospholipids and biogenic amines. Several scientific studies indicate that SAMe may be useful in the treatment of depression.

5-Hydroxytryptophan (5-HTP) and tryptophan:

It is a natural product that contains high level of 5-Hydroxytryptophan (5-HTP) and tryptophan as a natural alternative to traditional antidepressants. When your body sets about manufacturing serotonin, it first makes 5-HTP. Taking 5-HTP as a supplement may raise serotonin levels. The evidence suggests 5-HTP and tryptophan are better than a placebo for alleviating depression. Considerable work has been devoted to the study of the mechanisms of antidepressant (AD) action, and it is now widely accepted that an increased central serotonergic (5-HT) neurotransmission constitutes a key therapeutic factor for depression.[12]

DOPAMINE:

It is a good source of the amino acid tyrosine. Tyrosine when converted into dopamine results in increased dopamine levels which in turn boosts mood. watermelon is fat free and contains a high amount of vitamin B6 that is used by the body to produce neurotransmitters like dopamine. DA may promote neurotrophic processes in the adult hippocampus as 5-HT and NA do.

It is thus possible that the stimulation of multiple signalling pathways resulting from the elevation of all three monoamines may account in part for an accelerated and greater antidepressant response.[13]

B Vitamins:

B vitamins play a role in the production of certain neurotransmitters, which are important in regulating mood and other brain functions. Folic acid deficiency has been noted among people with depression. Vitamin B6, or pyridoxine, is the cofactor for enzymes that convert L-tryptophan to serotonin, so vitamin B6 deficiency might result in depression and there is some evidence that people with depression respond better to treatment if they have higher levels of vitamin B12.

Thus, the present work though of preliminary in nature suggests that the aqueous extract of Citrullus lanatus has good antidepressant activity.[14,15] Further elaborate research work involving more numbers of animals and different experimental models of antidepressant activity are needed to elucidate the exact molecular and biochemical mechanism of action to develop more effective compound.

CONCLUSION:

Despite the wide use of synthetic drugs to treat depression, these drugs often associated with adverse effects and limitations. The search for a natural product with fast onset of action, wide safety margin and less side effects has come to attention. Hence this study was undertaken to evaluate the anti-depressant effect of fruit of *Citrullus lanatus* The antidepressant activity is attributed due to the presence of polyphenols, flavonoids in the extract. Another possible mechanism of action is the attenuation of oxidative stress produced during depression, by the polyphenols and tannic acid present in extract. Aqueous extract contains lycopene has been reported to possess cytoprotective effects on account of its antioxidant activity by reducing lipid peroxidation and also significantly scavenges superoxide as well as inhibits its generation. Aqueous extract of fruits of has been found to be potent antioxidants in vitro.

The effective components of *Citrullus lanatus* that have antidepressant-like effect includes S-adenosylmethionine, dopamine, B-vitamins, 5-hydroxytryptophan (5-htp) and tryptophan. Hence its effect is almost similar to that of standard drug. However, the exact mechanism of action could not be analyzed due to presence of various phytochemicals. Further studies are required to characterize the exact mechanism of anti-depressant effect of *Citrullus lanatus*.

REFERENCES

1. Katon and Sullivan. Depression and chronic medical illness. Journal of Clinical Psychiatry. 1990; 51 Suppl-3:11-14.
2. American Psychiatric Association. DSM-IV TR. Washington, D.C. APA; 2000 with permission as reproduced in Sadock BJ, Sadock VA, Ed., Synopsis of psychiatry, 9th ed., New York: Lippincott Williams & Wilkins; 2003. p.542.
3. Solomon DA, Keller MB, Leon AC, Mueller TI, Lavori PW, Shea MT, et al. Multiple recurrences of major depressive disorder. Am J Psychiatry. 2000; 157(2):229-33.
4. Collins, J.K. et al. Watermelon consumption increases plasma arginine concentrations in adults. Nutrition , 2007; 23:261–266.
5. Perkins-Veazie, P., Collins, J.K., Davis, A.R. & Roberts, W. Carotenoid content of 50 watermelon cultivars. J. Agric. Food Chem., 2006; 54: 2593–2597.
6. Rahman A.H.M.M., Anisuzzaman M., Ferdous Ahmed, Rafiul Islam A.K.M. and Naderuzzaman A.T.M.. Study of Nutritive Value and Medicinal Uses of Cultivated Cucurbits, Journal of Applied Sciences Research, 2008; 4(5): 555-558.
7. Loiy Elsir Ahmed Hassan. In-vitro Antimicrobial activities of chloroformic, hexane and ethanolic extracts of Citrullus lanatus var. citroides. Journal of Medicinal Plants Research. 2011; 5 (8): 1338- 1344. 15. Loiy Elsir Ahmed Hassan. In-vitro Antigiardial activity of Citrullus lanatus var. citroides extracts and cucurbitacins isolated compounds. Journal of Medicinal Plants Research 2011; 5 (15):3338- 3346.
8. Naresh Singh Gill. Evaluation of Antioxidant activity of citrullus lanatus Seed extract in Rats. Latin American journal of pharmacy (formely Acta Farmaceutica Bonaerense), Lat. Am. J. Pharm. 2011; 30(3):429-34.
9. Sevcan Altas, Göksel Kızıl, Murat Kızıl, Aydın Ketani, Parvez I. Haris, Protective effect of Diyarbakır watermelon juice on carbon tetrachloride-induced toxicity in rats. Food and Chemical Toxicology, 2011; 49: 2433–2438
10. Okunrobo O. Lucky, Uwaya O. John, Imafidon E. Kate, Osarumwense O. Peter, Omorodion E. Jude, Quantitative determination, Metal analysis and Antiulcer evaluation of Methanol seeds extract of Citrullus lanatus Thunb (Cucurbitaceae) in Rats. Asian Pacific Journal of Tropical Disease
11. Suominen KH, Isometsa ET, Henriksson MM, Ostamo AI, Lonnqvist JK. Inadequate treatment for major depression both before and after attempted suicide. Am J Psychiatry. 1998; 155(12):1778-80.
12. 5 .Sullivan PF, Neale MC, Kendler KS. Genetic epidemiology of major depression: review and meta-analysis. Am J Psychiatry. 2000 Oct; 157(10):1552-62.
13. Fauci AS. Harrison's principles of internal medicine / editors, Anthony S. Fauci... [et al.]. 17th e.d. New York: McGraw-Hill Medical; 2008; p. 2717- 18.
14. Sivarajan VV, Indira Balachandran. Ayurvedic Drugs and Their Plant Sources. Oxford and IBH Publishing Company, New Delhi, India. 1994; 289-90.
15. Lele RD. Four new approaches for validation of Ayurvedic herbal drugs. Int J Ayurveda Res. 2010 Jul-Sep; 1(3): 136–37.