Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/p4fw5b90

POTENTIAL APPLICATION OF PHYSALIS PERUVIANA WITH COMPARISON OF IMIPRAMINE.

Syed Uzair Hasan[1], Syeda Afroz[2*], Sana Imran[3], Abdul Ghaffar[4], Faiza Khan[5], Rushdah Fatima Siddiqui [6], Areeba Ashfaque[7], Syeda Areeba Naqvi[8]

[1]Department of Pharmacology. Faculty of Pharmacy and Pharmaceutical Sciences. UOK
[2*]Department of Pharmacology Faculty of Pharmacy and Pharmaceutical Sciences. UOK
safroz@uok.edu.pk
[3]Department of Pharmacology, Jinnah Sindh Medical University, Karachi, Pakistan.
[4]Department of Pharmacology, Faculty of biological, Pharmaceutical and health sciences. UOB
[5]Dr Ruth KM Pfau Civil hospital karachi.Pakistan .
[6]Department of Pharmacology. Faculty of Pharmacy and Pharmaceutical Sciences.UOK
[7]Department of Pharmacology. Faculty of Pharmacy and Pharmaceutical Sciences. UOK
[8]Department of Pharmacology.Faculty of Pharmacy and Pharmaceutical Sciences. UOK

***Corresponding Author:** Dr.Syeda Afroz
[*]Department of Pharmacology. Faculty of Pharmacy and Pharmaceutical Sciences.
safroz@uok.edu.pk

Abstract
The current study aimed to evaluate the pharmacological potential of fresh fruit juice of the *Physalis peruviana* (FFJPP) for the antidepressant effect in mice using tail suspension tests(TST) and forced swim test (FST) methods. The fresh fruit was purchased from the local market and the experiment was carried out in mice using a behavioral model i.e. tail suspension test and forced swimming test. The fresh fruit of *Physalis peruviana* was cut into small pieces, blended in a blender, and squeezed with a mulmull, and filtrate was obtained. The mice of either gender were randomly divided into five (5) groups, six in each group, acclimatized for one week before starting the experiment, and had free access to laboratory food and water. The experimental test was conducted in the Department of Pharmacology with approval from the Department of Pharmacology Ethical Committee. The fresh fruit juice of the *Physalis peruviana* plant was administered orally to the experimental groups for 14 days using tail suspension tests (TST) and forced swim test (FST) and immobility time was recorded. The data was analyzed using one-way ANOVA by applying Dunnett's multiple comparisons test in Graph Pad prism 8.1 and expressed as Mean ± SEM. The $p<0.05$ was considered as statistically significant. The results showed a significant decrease in immobility time in both the standard group (imipramine 10mg/kg) and extract treated at the dose of 2ml/kg and 3ml/kg) of body weight compared to the control group. In conclusion, the fresh fruit juice of *Physalis peruviana* (FFJPP) showed an anti-depressant effect in mice. It may be further suggested that further evaluation of mechanisms of antidepressant potential at the molecular level in animal models using advanced and modern technology.

Keywords: *Physalis peruviana*, Antidepressant effect, Mice, TST, FST

The World Health Organization (WHO) states that neuropsychiatric diseases are putting increasing pressure on the nation's healthcare system, social order, and economy. Nowadays, there are numerous approaches to reduce the likelihood of these conditions occurring as well as therapies or ways to enhance their symptoms. Antidepressants are the major kind of medication used to treat depression. These drugs can also be used to treat non-medical disorders like pain, anxiety, or insomnia. The fact that certain antidepressants have side effects that the patient may find intolerable is one of their drawbacks. Using medicinal plants could be one encouraging strategy in this area. Numerous phytochemicals found in plant parts have the potential to benefit mental illnesses by interacting with a range of targets[1].
Depression is a psychological disorder that has a significant effect on an individual's feelings, behavior, and thoughts. It causes symptoms such as anhedonia and low mood, anxiety and irritability, loss of energy, changes in appetite and sleep patterns, and sporadic suicidal thoughts. The main cause of depression is stress, which comes in many forms and is a permanent part of daily life. These types of stress include environmental, mental, physical, and emotional stress [2].

The “American Psychiatric Association” and the “World Health Organization” have both well-known various types of depression in their respective classifications of diseases and mental health disorders. An episode of depression can be categorized as a) moderate depression, b) major depression, or c) bipolar affective disorder, depending on the severity and quantity of symptoms. The “National Institute of Mental Health (NIMH)” also categorizes depression in various forms, such as “Major Depression, Persistent depressive disorder, Perinatal depression, and Seasonal affective disorder” [3]. According to the reports of WHO 2024, Approximately three point eight percent of the general people suffer from depression, with 5 percent of adults 4 percent of men, and 6 percent of women), as well as 5.70 percent of those older than 60 years. About 280 million individuals worldwide are affected by depression (1). Depression is approximately fifty percent more predominant in females than in males. Depression distresses over ten percent of gestational women and those females who have in recent times given birth globally (2) over 700 hundred thousand individuals die per annum as a result of suicide. Regardless of the availability of proper and effective treatments for psychological disorders, over 75 percent of individuals in developing countries are not given any form of management (3). Hurdles to providing proper and effective care consist of inadequate funding for mental health care, a lack of skilled healthcare professionals, and the social humiliation associated with psychological illnesses [4].

Medicines of plant origin are widely utilized and have seen a growing presence in both traditional and modern medicinal practices, particularly in developing nations. *Physalis peruviana* is recognized as one of the most commonly utilized plants in global conventional medicine. Several countries across the globe incorporate *Physalis peruviana* into their traditional medicinal systems to address a variety of health concerns, with a particular focus on managing diseases and gastrointestinal tract disorders (25.3 percent). The leaf was the most frequently utilized component, accounting for 49.28 percent of usage. It was primarily prepared through decoction (31.6 percent) and predominantly administered orally (53.6 percent) as the main method of intake. A total of five hundred and tow phyto-constituents were identified in various plant parts, with the highest concentration (38.2 percent) found in the ethanol/ethyl acetate extract of the fruit.

Multiple classes of phytochemicals were identified in the plant, with particular prominence given to terpenes (26.1 percent) and phenolic compounds (14.9 percent). Esters were also found in high abundance, comprising 11.56 percent of the total compounds. Carotenoids were the most prevalent in the terpenes category at 11.1 percent, followed by monoterpenes at 8.7 percent and di-terpenes at 3.18 percent. Nevertheless, flavonoids make up 5.18 percent of the reported phenolic compounds, followed by cinnamic acid derivatives at 3.4 percent, mono-phenolic compounds at 1.8 percent, and phenolic acids at 1.33 M. Hexadecanoic acid (palmitic acid) was the most cited (five times). *Physalis Peruviana*

is vital for disease management in certain countries and contains many chemical compounds used for multiple mild to moderate illnesses worldwide [5].

Material and Methods

Study Design

The current study was conducted on Physalis peruviana fresh fruit juice, which was investigated for its antidepressant properties using animal models such as mice.

Plant Materials

The fresh *Physalis peruviana* fruit was bought from the local markets in Karachi, Pakistan and identified by Dr. Syeda Afroz, Associate Prof, Department of Pharmacology, University of Karachi.

Preparation of Fresh Physalis Peruviana Fruit Juice

Making fruit juice involves weighing the plant's fruit, processing it in a blender, and storing it in dried and cleaned containers. Four hundred and fifty grams of fresh, completely ripened fruits were chopped into small pieces and blended for two minutes. With the help of muslin fabric, the pulp was squeezed and extract juice was obtained, which was then chilled and given to experimental animals for antidepressant research. Just before administration, each medication solution was newly prepared [6].

The Chemicals and Apparatus

The Department of Pharmacology provided the laboratory facilities, and analytical-grade chemicals, equipment, and solvents were employed in the investigation.

Animals

Groups of three (3) Swiss albino mice, weighing between 26 and 32 grams, were kept in hygienic polypropylene cages. At 24 ± 5 ºC ambient temperature, a 12:12 hour dark/light cycle was observed. The experimental animals were housed in the Departmental animal house at the Department of Pharmacology, University of Karachi, under standard hygienic conditions throughout the research period. They were given a week to acclimate before the experiment began and had access to water, and laboratory feed at room temperature.

Grouping of the Animals

Five (5) groups of six animals each were formed from the distribution of the animals which are as follows:

- Group-1 Control/ Normal Saline group
- Group-2 standard (imipramine 10mg/kg)
- Group-3 extract treated with FFJPP 1ml/kg of body weight
- Group-4 extract treated FFJPP 2ml/kg of body weight
- Group-5 extract treated FFJPP 3ml/kg of body weight

Assessment of Anti-Depressant Activity

For the assessment of the antidepressant effect of *Physalis peruviana*, the study was designed using an animal model. The most common method for assessing the antidepressant effect of natural compounds in animal models is by observing the behavioral signs. Resignation-related indicators, also known as "behavioral despair" or "learned helplessness," are the main behavioral measures used in the learned helplessness model and antidepressant efficacy screening tests like the forced swim and tail suspension tests. During the initial two assessments, the absence of movement caused by being subjected to an unavoidable unpleasant situation (such as being forced to swim or suspended by the tail) is utilized as a sign of surrender. Within the framework of the learned helplessness model, animals, typically rats, are subjected to unavoidable foot shocks. The animals display "helplessness" when they fail to learn how to escape when their environment is changed to allow for escape [7].

By Tail Suspension Test Method

The most common method used for the antidepressant properties of natural compounds is tail suspension test in rodents which was an effective approach for examining the plant extract's antidepressant impact. In this study, a mouse is hung by its tail (one centimeter from the tail's tip) and fifty centimeters above the ground using a secure tape for five minutes. The period in which each mouse remained motionless (immobility) was subsequently noted [8].

By Forced Swim Test Method

The forced swim test is extensively utilized as a common assay for investigating depression-like behavior in rodents. The Forced Swim Test operates under the premise that, when placed in a water-filled container, an animal will initially attempt to run away but will ultimately display immovability, which might be interpreted as indicative of behavioral despair. This test has been widely utilized due to its inclusion of the exposure of animals to stress, which has been demonstrated to be a factor in the susceptibility to major depression. This method is based on the principle of measurement of immobility time (seconds), and is carried out to observe the locomotor activity of the mice that are placed in an experimental pool of water [9].

Statistical Analysis of Data

The data of our study was examined via one-way ANOVA by applying post hoc Dunnett's multiple comparisons test in Graph Pad prism 8.1 and represented as Mean ± SEM. The value $p<0.05$ was considered significant.

Ethical approval

The current study was carried out on animal models after obtaining ethical endorsement and authentication from the "Ethical Committee of Animal" Department of Pharmacology, Faculty of Pharmacy and Pharmaceutical Sciences (FPPS), University of Karachi, Sindh, Pakistan.

Result of Forced Swim Test (FST)

The most common method for the assessment of the anti-depressant effect of a natural compound in an animal model is the of behavioral assessment of rodents. A forced swim test (FST) and a tail suspension test (TST) were used in this study to evaluate the anti-depressant effect of Fresh Fruit Juice of *Physalis Peruviana.* The result of the forced swim test showed a substantial decrease in the immobility time of both the standard and extract treated in mice as compared to the control group.

Significant reduction in immobility period in the standard group (63.166±1.6***) and extract treated at a dose of 2ml (189.5±6.16*), and 3ml/ kg (94.56±.13**) of body weight respectively as compared to the normal control group, as listed in Table 4.1.

Table No.4.1 Effect of fresh fruit juice from *Physalis peruviana* (FFJPP) in FST method on the immobility time of mice

S. No	Treatment	Immobility time period	
		Forced swim test (FST)	
		Day 1 Mean ± SEM	Day 14 Mean ± SEM
2	Control Group	220.6±3.21	217.3±3.36
3	Imipramine 10mg/kg	191.3±2.5	63.166±1.6***
4	FFJ of PP 1ml/kg	221.5±0.51	221.8±0.61
5	F.J of PP 2ml/kg	192.8±7.04	189.5±6.16*
6	FFJ of PP 3ml/kg	121.0±3.94	94.56±.13**

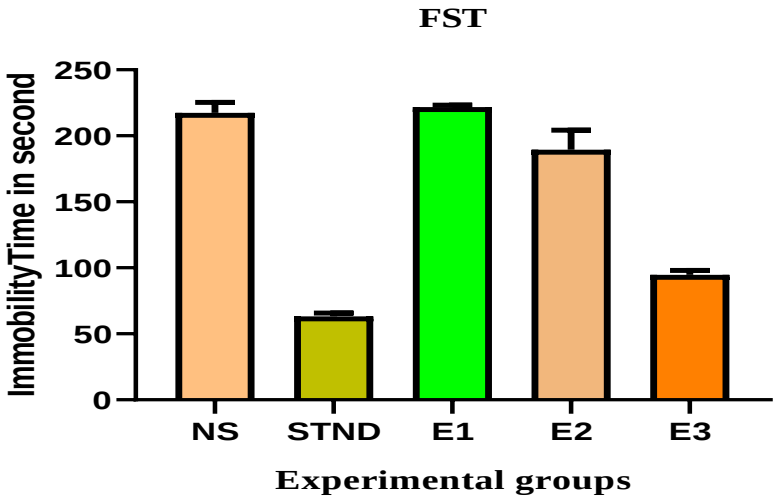

Figure.4.1 Effect of fresh fruit juice from *Physalis peruviana* (FFJPP) in FST method on immobility time of mice

Result of effect of immobility time of mice in Tail Suspension Test (TST)

The results of the current study showed a considerable reduction in the immobility time of mice in the tail suspension test method in both the standard and extract treated in mice as compared to the control/ normal Saline group. Significant decrease in immobility time in the standard group (90.333±3.10***) and extract treated in 2ml/kg (186.0±3.02*) and 3ml/kg (111.83±2.31**) as associated with the normal control/ Normal Saline group, as listed in Table 4.2.

Table No. 4.2 Effect of fresh fruit juice of *Physalis peruviana* (*FFJPP)* in TST method on immobility time of mice

S. No.	Treated groups	Immobility time (Seconds) Tail Suspension Test (TST)	
		Day 1Mean ± SEM	Day 14Mean ± SEM
1	Control Group	303.5±1.5	273.16±0.96
2	Imipramine 10mg/kg	183.33±0.9	90.333±3.10***
3	F.J of PP 1ml/kg	215.8±2.6	215.6±3.10
4	F.J of PP 2ml/kg	214.0±2.04	186.0±3.02*
5	FFJ of PP 3ml/kg	215.333±1.26	111.83±2.31**

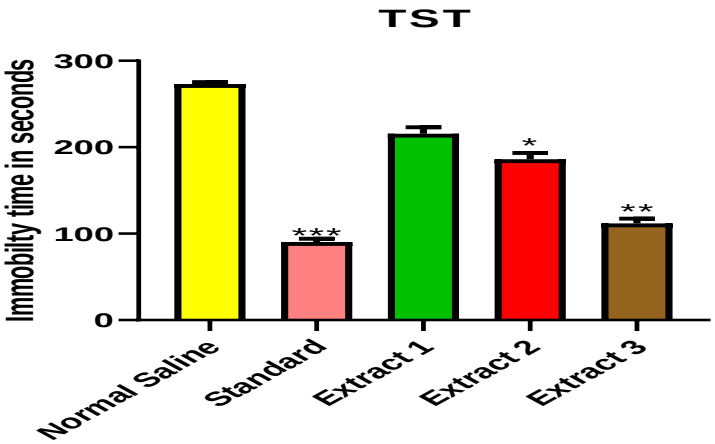

Figure 2 Effect of fresh fruit juice from *Physalis peruviana* (FFJPP)in TST method on the immobility time of mice

Discussion

Depression treatment requires an extended period to get an optimal response; therefore, it is imperative to execute not only acute but prolonged administration of crude drugs to animal models. The current study was carried out on an animal model to assess the anti-depressant potential of *Physalis peruviana* in mice. The results of this study indicated that the oral administration of fresh fruit juice extract of *Physalis Peruviana* at a dose of 2ml and 3ml exhibited substantial antidepressant effects compared to the normal control and standard drug imipramine 10mg/kg of body weight. The result of the current study represented that the fresh fruit juice of *Physalis peruviana* had significantly decreased the immobility time in both standard and extract-treated animals. It was observed that after fourteen days of treatment, the FFJPP produced an anti-depressant effect at the dose of 2ml/kg and 3mlmg/kg of body weight in the tested models whereas, no significant changes were observed at low doses of 1ml/kg in the test animals.

A similar study was carried out in mice for the anti-depressant potential of fresh fruit juice of *Malus domestica,* and the outcomes showed a substantial reduction in both immobility time and monoamine oxidase in the brain in chronic administration of FFJMD at dose 1ml/kg and 2ml/kg in mice [10]. Similarly, our study showed a substantial reduction in immovability time in FST and TST methods at doses of 2ml/kg and 3ml/kg compared to control and standard groups respectively of test animals.

According to the previous literature review that has clearly indicated a connection between oxidative stress and the pathophysiology of major depression. It revealed a substantial correlation between the severity of depression and the levels of erythrocyte superoxide dismutase/lipoperoxidation. In the interim, the use of anti-depressants diminishes the oxidative stress associated with the depressive condition. Similarly, the previous literature suggests that *Physalis Peruviana* fruit juice has antioxidant activity. Therefore, the antioxidant activity of the fresh fruit juice from Physalis P may contribute to its antidepressant-like effects [11].

The result of the current study revealed that fresh juice of *Physalis peruviana* fruit consume a significant effect on depression after oral administration at the dose of 2ml/kg and 3ml/kg as compared to the control and standard using the FST and TST method in mice. Immobility in TST is a reflection of a hopeless mood that can be lessened by several drugs that are useful as therapies for depression in people. Similarly, in the Forced swim test, the mice are obliged to swim in a small area, they are incapable of running away. Latency until the initial entry and the HBT head dip response were observed. This is supposed to cause animals to experience behavioral despair, a condition that mimics sadness in humans. Compared to the FST and HBT, the TST has reportedly been found to be less stressful and to have a higher pharmacological sensitivity. Therefore, because Physalis Peruviana reduces mice's immobility time, the current study suggests it may be helpful for depression.

Conclusion

The current study was aimed to evaluate the anti-depressant effect of fresh juice extract of *Physalis Peruviana* fruit in rodents. The oral administration of Fresh juice of *Physalis Peruviana* (FFJPP) fruit at the dose of 1ml/kg, 2ml/kg, and 3ml/kg respectively to mice for the period of fourteen days, showed a substantial reduction in immobility period compared to the control in both TST and FST methods. On observation of the behavior, a substantial reduction of the immobility period was observed during the experiment, indicating the anti-depressant effects. Thus the current study represented that fresh juice of *Physalis peruviana* fruit possesses an Anti-depressant effect in animal models and could be used as a folklore tradition medicine for mild to moderate depression.

Recommendation

The previous literature has shown the medicinal importance and the wide-ranging properties of the *Physalis peruviana* plant It may be further suggested that further evaluation of mechanisms of antidepressant potential at the molecular level in animal models using advanced and modern technology.

References

1. Avram, S., et al. *The study of natural compounds as antidepressants by bioinformatics methods*. in *Biology and Life Sciences Forum*. 2021. MDPI.
2. Sinyor, M., J. Rezmovitz, and A. Zaretsky, *Screen all for depression*. 2016, British Medical Journal Publishing Group.
3. Torrey, E.F., W.W. Simmons, and L. Dailey, *The NIMH Research Portfolio: An Update.* The Primary Care Companion for CNS Disorders, 2023. 25(4): p. 48200.
4. Abdoli, N., et al., *The global prevalence of major depressive disorder (MDD) among the elderly: A systematic review and meta-analysis.* Neuroscience & Biobehavioral Reviews, 2022. 132: p. 1067-1073.
5. Kasali, F.M., et al., *Ethnotherapeutic uses and phytochemical composition of Physalis peruviana L.: an overview.* The Scientific World Journal, 2021. 2021(1): p. 5212348.
6. Jeamsrichai, T. and M. Sang-ngern, *Development of physalis peruviana l. fruit Extract as antioxidant and UV absorption agent and its application in sunscreening product*. 2017, Mae Fah Luang University.
7. Mankar, S.S., et al., *Antidepressant in animal models of depression and study of cognitive property.* GSC Biological and Pharmaceutical Sciences, 2019. 7(3): p. 064-076.
8. Rahman, S.U., et al., *Antidepressant, anxiolytic sedative and muscle relaxant activities of Nicotiana plumaginifolia in mice.* PHYTONutrients, 2023: p. 09-18.
9. Yankelevitch-Yahav, R., et al., *The forced swim test as a model of depressive-like behavior.* JoVE (Journal of Visualized Experiments), 2015(97): p. e52587.
10. Lobo, A.R. and S. Satish, *An investigation on anti-depressant activity of fresh fruit juice of Malus domestica in experimental animal models.* Int. J. Res. Pharm. Pharm. Sci, 2019. 4(1): p. 19-23.
11. Wu, S.-J., et al., *Antioxidant activities of Physalis peruviana.* Biological and Pharmaceutical Bulletin, 2005. 28(6): p. 963-966.